Histological Contributions:

The Blood Vessels;
The Alimentary Canal;
The Urinary Excretory Passages;
The Suprarenal Capsules;
The Mammary Gland.

BY

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CHAPTER XI.

THE BLOOD-VESSELS.

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In man, a closed circuit of branching tubes, which proceed from a central organ, the heart, and, ramifying throughout the body, return the blood to this central organ, constitutes the blood-vascular system, as it has been named.

Of these vessels we recognize three different kinds: arteries, capillaries, and veins. The arteries convey the blood to the various capillary districts, whence it is again collected and carried back to the heart by the veins.

The arteries, highly elastic throughout, are composed of three superimposed layers or tunics. The veins, less elastic, and consequently more flaccid and compressible, likewise consist of three coats or tunics. In both sets of vessels these coats have received the names of *intima* for the inner, *media* for the middle, and *adventitia* for the external layer. The capillaries, intervening between the two, form minute branching tubules, which generally have but a single exceedingly thin and permeable membrane as the sole constituent of their walls.

Of course, all these vessels merge into one another, so that a sharp line of demarcation can nowhere be drawn; but in their typical forms they present clearly defined structural differences, necessitating a separate description of them. We begin with the simplest and yet most important class:

The capillary blood-vessels.—They are composed, as we have already said, of a single layer of cells, arranged in tubular form, and containing nuclei. These corpuscles are directly continuous, on the one hand, with the inner coat of

the terminal arteries, and, on the other, with the intima of the veins, hence also with the lining membrane of the heart. They are called *endothelia*, and since they constitute the only structural elements which enter into the composition of all blood-vessels, we will first consider them and their relations to these vessels.

The vascular endothelium.—Histologists understand by the term *endothelium* a thin layer of flattened cells lining the free surface of various membranes, canals, sheaths, and cavities, all belonging to the serous type. *Epithelium*, on the other hand, is found covering the skin and mucous surfaces. All endothelia, in common with the blood, the blood-vessels, and connective tissues, are derived from the *mesoblast*, or middle of the three fundamental layers of the embryo. The epithelia, it will be remembered, originate in the two other layers, called *epiblast* and *hypoblast*, respectively—the former being the superior and the latter the inferior layer of the embryo.

In adult human subjects the vascular endothelia are made up of thin, polygonal, sometimes irregularly pentagonal, flattened cell-plates. Most of the elements are furnished with a rounded or ovoid nucleus, of central or more or less peripheral location (Fig. 58). Some have two nuclei. In general, the cells are somewhat elongated in the longitudinal direction of the vessel to which they belong. They also grow slightly narrower as the calibre of the vessel decreases. Their borders are serrated or scalloped, and dove-tailed into one another. An albuminoid substance, ordinarily invisible, cements their adjoining edges. This substance has the peculiar property of effecting an energetic reduction of silver nitrate. Hence, by proper management, the outlines of each individual cell may be made visible as a black zigzag surrounding a nucleus. Every cell represents a plate-like expanse of modified protoplasm. Remnants of this original substance may be seen to surround the nuclei of young vessels, where they appear in the shape of varying quantities of distinctly granular matter. Klein has described an *intracellular network*, formed by plexuses of minute fibrils, and associated with a second denser reticulum within the nucleus, called the *intranuclear network*. Whatever interpretation we choose to give these minute structures, the fact of their existence is indisputable. In man, however, their presence is not as readily demonstrable as in animals.

An isolated endothelial cell, when tilted up on its edge, presents the appearance of a straight or curved double contour, with a central thickening corresponding to its nucleus. Viewed *en face*, we observe the sinuous outline and the central or eccentric nucleus, with its surrounding granules of protoplasm. The shape and contour of endothelial cells are subject to con-

FIG. 58.—Endothelium of the carotid artery of man, after treatment with nitrate of silver: *a*, cells; *b*, clearer, *c*, darker intermediate spaces; *d*, intra-cellular circular and spotted markings. Eberth.

siderable variations in the different vascular districts. Such differences also occur in the same district, with the varying degree of expansion or contraction of the particular vessel under observation.

The capillaries proper.—In point of wideness of distribution, this variety of blood-vessels greatly exceeds all others. Indeed, the capillaries occupy a rank, in this respect, second only to the connective-tissue group of histological structures. As regards importance to the economy, it will only be necessary to advert to the vital processes of nutrition, secretion, respiration, and excretion, to recall the quality and extent of their physiological usefulness. Throughout the

body[1] capillary plexuses are interposed between arteries and veins, which constitute a series of conveying and returning tubes. Thereby the direct continuity of these blood-channels is established.

It is in these intermediate territories, and in them only, that the blood serves its true function of giving and taking. True markets of exchange, then, these capillary districts, where the system is supplied with new material, and in return gets rid of useless or even deleterious by-products of tissue-life. Hence, the paramount importance of these vessels in the maintenance of life and health. Hence, also, the direct practical utility of knowing their minute anatomy and physiological dignity. Every practitioner of medicine will see the important relation this branch of histology holds to pathology, and therefore to therapeutics. At the same time we should not forget that the *rôle* played by the capillaries in the system is normally due to the inherent mechanical and physical properties of a finely elastic animal membrane, rather than to any specific action of their cellular constituents.

FIG. 59.—A rather large capillary from the hyaloid of the frog, presenting a membranous and nucleated tunica adventitia. Eberth.

Robin, following Henle's example, distinguishes several varieties of these vessels. It seems to me proper to limit the term capillaries to those minute tubules which are entirely devoid of muscular elements. This corresponds to the classification adopted by Virchow, Kölliker, Eberth, Ranvier, Frey, and others. It is the one therefore that has generally been accepted, and is both simple and logical.

The diameter of these tubules varies from 0.0045 to 0.0115 mm. Their structure is readily understood. Examined in the living animal with a high power, we see merely a delicate, hyaline, double-contoured membrane, having an

[1] Hoyer has shown that a direct communication of arterioles with venules occurs normally in the tips of the fingers, the matrix of the nails, the tip of the nose, and various other parts.

average thickness of 1 to 2 micro-millimetres (0.001—0.002 mm.). This membrane forms a tubule, the parietes of which are studded at intervals with rounded or oval nuclei, often containing one or more bright nucleoli. When oval, these nuclei have their long axis parallel with the direction of the vessel. Their average size is 0.0056 to 0.0074 mm. They possess the property of eagerly imbibing most of the staining fluids employed in histology, and of resisting the action of dilute acids, alkalies, and other reagents. (See Fig. 59.)

Besides nuclei, the capillary wall contains at various points peculiar granules, which indicate its protoplasmic nature. In addition, Stricker and Eberth have described lateral processes and pointed prolongations jutting out from the parietes of the

FIG. 60.—Capillaries of the lungs of the frog, with irregularly dentated cells: *a*, vascular meshes. Eberth.

capillary tubes. In growing tissue these are readily demonstrable, often forming thread-like connecting bridges between neighboring vessels; at a later period they are hollowed out into true capillaries. The shorter sprouts are also protoplasmic buds, capable of further development into similar vessels. (See Fig. 61.) By employing weak solutions of silver nitrate, the capillary-wall may be shown to consist of variously shaped areas, each one corresponding to a nucleated cell. They are the endothelia, and represent, as already stated, the sole essential constituents of all capillaries. Their form varies with the calibre of the vessel, the smaller capillaries being composed of

corpuscles which are comparatively narrow, the larger vessels having broader cells. In man they have an average length of 0.0756—0.0977 mm., and an average breadth of 0.01—0.05 mm. The intercellular boundaries, brought out as dark lines by means of the silver salt, frequently exhibit little nodular swellings. (See Fig. 58.)

In addition to the ordinary endothelia, we find smaller areas, generally without nuclei; they have rounded or somewhat dentate contours, and are interposed between the other cells. Eberth believes that some of these *intercalated areas*, as Auerbach has called them, probably correspond to portions of strangulated vascular cells. It is more logical to regard them as the remnants of an incomplete endothelial desquamation, a process which is of physiological occurrence throughout the blood-vessels. These remaining bits are finally destined to become quite detached from the vascular wall, and are then swept away by the rush and flow of the blood-current. The detached portions of such endothelia and their nuclei appear as free granules in the blood, where they have puzzled many observers, and have been variously called *microcytes*, *hæmatoblasts*, etc. From this description it is plain that Cohnheim's view, that these spaces are openings or stomata, is not sustained. True, we find in serous membranes of certain animals real openings, but these always appear of rounded shape, and are, to say the least, not commonly observed in human blood-vessels. This statement of the case does not militate against Cohnheim's well-known views that the corpuscles emigrate through the vessels, for, remembering the protoplasmic nature of the endothelial tubes,

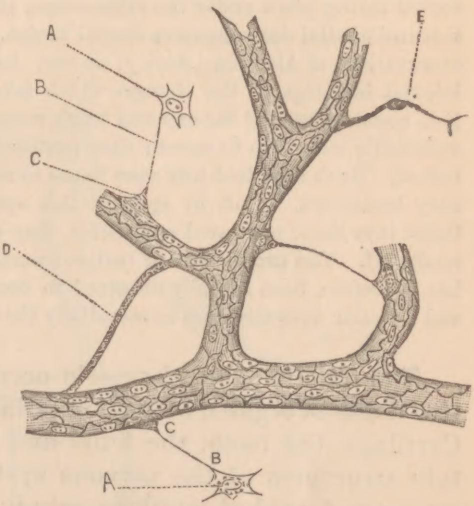

FIG. 61.—A, A, stellate connective-tissue cells connected by B, B, delicate protoplasmic threads to C, C, sprouts of endothelial tubes; D, protoplasm connecting two capillaries; E, nucleus imbedded in a primitive sprout of protoplasm, budding from wall of capillary. Specimen prepared by silver nitrate.

we can readily account for the phenomena in question. The capillary-wall is elastic, extremely thin, and permeable. By virtue of these qualities, it may allow the passage of a leucocyte or colored globule through its substance without suffering a permanent breach of continuity.

The writer's views on endothelial desquamation as a normal process of physiological import may strike the reader as insufficiently substantiated by known facts. But when we remember that similar processes have been actually observed taking place under the microscope, all doubts as to the probability of this endothelial desquamation should vanish. The author refers to the recent observations of Altmann (*Arch. f. mikros. Anat.*, Vol. XVI., p. 111). This histologist investigated the changes which take place in the serous epithelium (*i.e.*, endothelium) of the exposed frog's mesentery. Multiple swellings of the endothelia were seen to occur; then portions of these cells would become detached. Such detached bits were found to resemble in their appearance ordinary leucocytes. But, in spite of this apparent breaking up of the endothelia into these nucleated corpuscles, they often retained their individuality unaltered. The production of bodies resembling leucocytes from endothelia has, therefore, been actually observed in connection with serous membranes, and vascular desquamation is essentially the same process.

The capillary blood-vessels occupy the interstitial connective tissue of organs, without entering their parenchyma proper. Cartilage, the teeth, the hairs and nails, the cornea, and certain structures of the nervous system and organs of special sense are devoid of capillary supply.

Most of the larger tubes are invested by a delicate, external, sheath-like structure, called the *capillary adventitia* or *vascular perithelium*. It is composed of a rather close network of delicate connective-tissue fibrils. Prolongations of peculiar stellate cells, which clasp the capillary-tube, may sometimes be seen to join these fibrils. (Fig. 62.) Such branching cells are also encountered at some distance from the capillaries. They show delicate processes, which may anastomose with the offshoots of the adventitial corpuscles. In other places we only find external plates of connective-tissue cells (Krause's *inoblasts*), which have become more or less fused with the capillary-wall. In many instances the perithelium is inseparable from the connective-tissue stroma surrounding the vessel.

In reference to the manner of anastomosis, the forms and modes of ramification of different networks vary with the different tissues and organs of the body. Hence, a simple in-

spection of capillary reticula will generally enable us to decide the nature of the tissue or organ in question. From a physiological point of view, we recognize a causal relation between high capillary development and great functional activity. Therefore, the abundance of capillaries will determine the physiological importance of an organ.

The chief forms of ramification may be grouped as follows: 1. Loops (*a*), simple or compound; *e.g.*, the skin and the hard

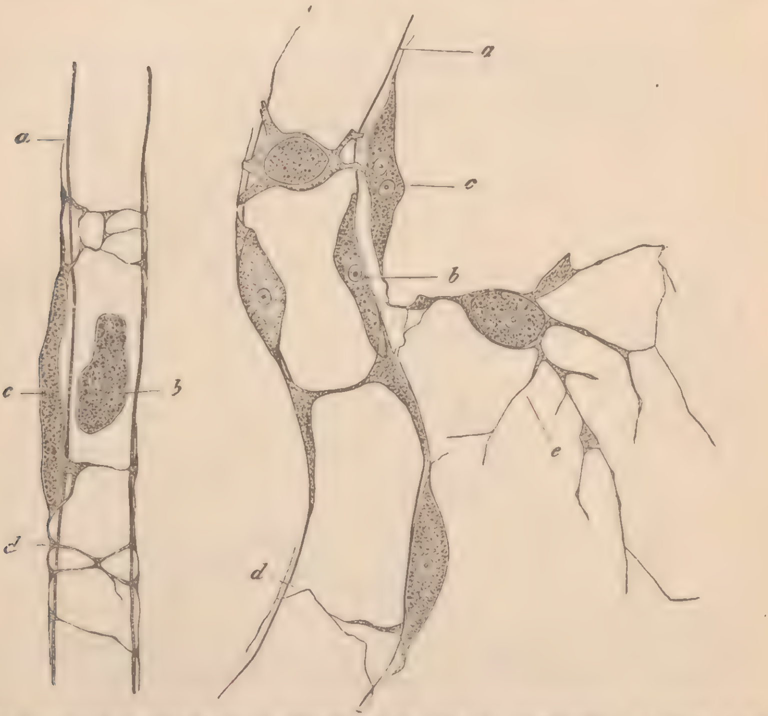

FIG. 62.—Capillaries from the hyaloid membrane of the frog: *a,a*, capillary-wall; *b,b*, nuclei of the same; *c,c*, cells of the tunica adventitia; *d,d*, processes of these cells clasping the capillary-wall; *e*, stellate cell anastomosing with the cells of the tunica adventitia. Eberth.

palate; (*b*) reticulated (the intestinal villi). 2. Tufts (the kidney). 3. Irregularly polygonal networks (the glands and the mucous membranes). 4. Rounded reticula, with round or polygonal meshes (adipose tissue). 5. Reticula with elongated meshes (the muscles, bones, and tendons). There would be a certain satisfaction in knowing that this or that vessel had a precise breadth, and its coat a certain thickness. The precision would be apparent, however, rather than real, because such

measurements vary greatly at different times in the same animal, and even more so in different animals. It may be stated, in general, that the calibre corresponds to the size of the largest blood-globules. In man, therefore, we have an average diameter of about 0.007 mm. The largest capillaries exist in the mucous membrane of the stomach and colon, the periosteum and bones, and the pituitary body. The smallest are found in the skin, the small intestine, the lungs, the muscles, the gray substance of the brain, and the retina (Valentin, Weber, and Henle).

The genesis, reproduction, and regeneration of capillaries.—There is still much uncertainty about the mode in which blood-vessels are first formed in the embryo. My personal

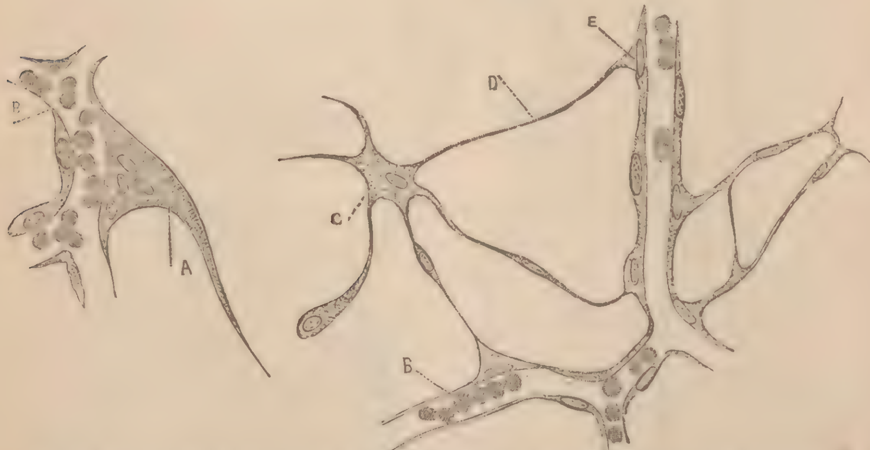

FIG. 63.—Growth and development of capillaries by nucleated sprouts of protoplasm: A, poly-nucleated large sprout with filiform process; B,B, blood-globules; C, branched cell; D, delicate protoplasmic tendril linking C with E, a smaller mono-nucleated sprout of endothelial wall.

observations on this subject, while working recently under the supervision of Kölliker, appear to confirm the view held by Foster and Balfour. These authors' account of the interesting process may be summed up as follows: About the second day of incubation in the chick, certain mesoblastic cells send out solid processes, which, uniting, form a protoplasmic network containing nuclei. A majority of the latter acquire a reddish tint, and are ultimately transformed into colored blood-globules. Other nuclei, however, remain unaltered, and, receiving an investment of protoplasm, form walls inclosing the reddened

nuclei. The protoplasm of these central nuclei rapidly becomes liquefied, thus forming the blood-plasma. And now we have a system of communicating tubules, containing corpuscles floating in a plasma, their walls consisting of nucleated cells. Hence, the blood-vessels do not arise as intercellular spaces, but are hollowed out to form channels in an originally solid reticulum of protoplasm derived from mesoblastic cells.

This explanation of the way in which vessels are formed aids us in understanding both how capillaries are reproduced in the adult, and their regeneration under pathological conditions. The capillary-wall itself, under the influence of favoring circumstances, begins to bud, as it were ; the delicate protoplasmic sprouts send out more delicate filaments, which, uniting with similar offshoots from neighboring vessels, establish a connection between two capillaries. In due time these solid structures undergo the familiar process of hollowing out, and the newly formed vessel is complete. Frequently the protoplasmic threads communicate, forming a reticulum which Ranvier has called *vasoformative network*. This author also observed that capillaries develop from special cells, termed *vasoformative cells*. They resemble leucocytes, and form by their prolongations a network of solid protoplasm. This is originally quite independent of already existing capillaries. Subsequently, however, a consolidation is effected, and the blood then flows through these new channels in the usual manner.

The author has been able to trace collections of emigrated leucocytes through various stages of progressive development, culminating in the formation of true capillaries. The experimental investigations on this subject were carried out in Professor v. Rindfleisch's laboratory, and have been fully described by his former assistant, Dr. Ziegler, of Würzburg.

The arteries.—If we follow the capillaries in a direction toward the heart, we soon find the endothelial tube receiving an investment of unstriped muscle-cells. These are wound transversely or obliquely around the capillary, thus forming a second tube, as it were, surrounding the first. External to the muscular layer there appears some connective tissue, mingling with which elastic elements may be observed. The direction of these additional fibres is mainly longitudinal. They form the third or external coat, called the *adventitia*, the second or

middle being represented by the muscle-cells, and the first or internal by the endothelial tube. The latter now receives the name of *intima*. When the layers of its walls are arranged in this simple manner the vessel is called an *arteriole*, and this constitutes the type of all arteries.

Arterioles, however, commonly contain a few additional fibres between the intima and the media, as the first indication of what afterward becomes a special layer. This structure, known as the *internal elastic coat*, attains considerable development in the larger vessels. With the growth of an artery in calibre its individual coats are reinforced by additional layers. Hence the thickness of the entire wall increases at the same

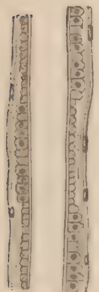

FIG. 64.

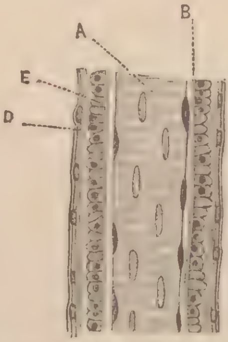

FIG. 65.

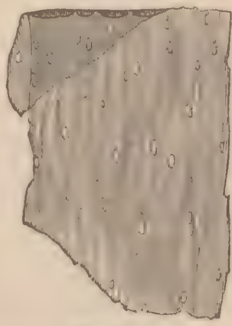

FIG. 66.

FIG. 64.—Minute artery showing optical section of alternate groups of muscle-cells, and an external nucleated membrane, representing the tunica adventitia.

FIG. 65.—A, intima; B, delicate internal elastic coat; E, media (as in Fig. 64); D, adventitia. Arteriole, from a child's mesentery.

FIG. 66.—Elastic internal tunic of the basilar arteries.

time that its structure is rendered more complex. But new tissues never appear. Moreover, the increased thickness is not uniformly proportionate to the enlarged calibre; neither does it take place by equal participation of the different tissues mentioned. In vessels of small and medium size there is a preponderance of muscular over elastic elements. In the larger trunks the reverse condition obtains. It is, therefore, proper to distinguish arteries of the muscular from those of an elastic type. The latter class is represented by the principal distributing trunks, all the remaining arteries belonging to the muscular type. There exist, however, no abrupt lines of demarcation between these main forms—the one merging gradually into the other.

The interposition of the *internal elastic coat* between the

intima and the media marks the transition of a minute into a small artery. This new layer consists at first of delicate fibrils of elastic tissue, or an apparently homogeneous membrane. Vascular contraction throws it into folds, which appear as longitudinal striæ or a transverse series of continuous festoons. As the vessel grows larger this coat gets thicker, becomes distinctly fenestrated, and presents a reticulated appearance. It is now made up of interlacing bundles of connective tissue and elastic fibres, with spaces left between them. The latter constitute the fenestræ of this layer, which in the large vessels becomes a double or triple lamellated membrane. Between it and the lining endothelium there appears still another structure, which has received various names from different authors. Thus, Kölliker has called it the *striated internal coat;* Remak, the *innermost longitudinal fibrous coat;* and Eberth, the *internal fibrous coat.* We shall employ the last term. The *internal fibrous coat* consists at birth of a granular substance, which becomes distinctly fibrillated in the adult. Embedded in this membrane lie numerous branching corpuscles, containing large, conspicuous nuclei. Besides these cells, smaller, so-called granulation-bodies are frequently seen. So far from regarding them as of pathological origin (Eberth, in "Stricker's Histology"), I prefer to consider them as matrix-cells for the regeneration of desquamated endothelia. My reasons for so doing are as follows: In the blood-vessels of young animals and newly born infants I have frequently noticed thick, dark, and granular bodies immediately below the endothelial lining. These subendothelial cell-plates were smaller and more polyhedral than ordinary endothelia, and invariably contained one or even two nuclei. They appeared to resemble germinating endothelial cells, such as Klein has described as occurring in serous membranes. They did not, however, occur in single layers, as Klein has seen them,

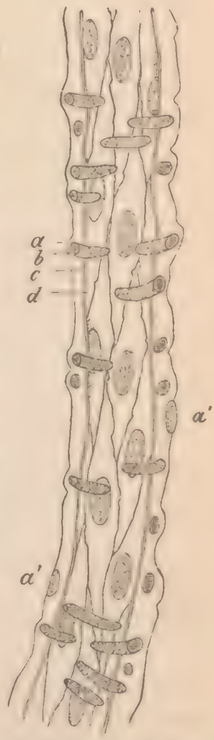

FIG. 67.—Small artery from the brain of man: *a*, tunica adventitia; *a′*, *a′*, nuclei of the tunica adventitia; *b*, muscle nucleus; *c*, elastic internal tunic; *d*, membrane formed of fusiform cells. Eberth.

but in strata. They were observed in particular vessels of young animals. It seems likely that these cells disappear or shrivel with the growth of the individual, but their sudden reappearance in pathological processes leads the author to believe that at least some of them persist through life. Talma (*Virchow's Arch.*, Vol. LXXVII., pp. 242–269) observed similar elements, but thinks they are derived from the ordinary endothelia, instead of *vice versâ*. He is also convinced that the latter are merely modified leucocytes; but this view has been shown to be erroneous by Virchow (*Archiv f. path. Anat.*, Vol. LXXVII., pp. 380–383). Endothelial desquamation is probably, as already stated, a physiological process of constant

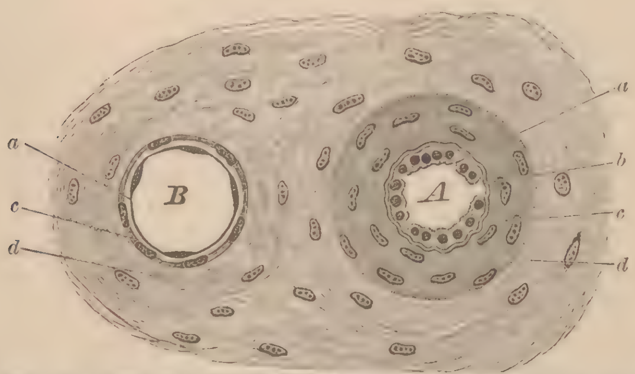

FIG. 68.—Transverse section through small artery and vein: *A*, artery; *a*, intima with bulging endothelial cells, the vessel being drawn in a state of contraction; *b*, internal elastic coat, wavy for same reason; *c*, media; *d*, adventitia. *B*, vein, same denominations.

occurrence, and in some respects analogous to the epithelial shedding from the surface of the skin and mucous membranes.

The *media musculosa*, or middle coat, consists of superimposed layers of smooth muscle-elements disposed in groups. Most of them lie transversely to the course of the vessel. The intervals between neighboring groups are occupied by connective tissue and elastic fibres, arranged in networks. This interstitial substance becomes augmented with the increasing calibre of the artery. In the largest trunks it all but replaces the muscle-cells. Here, however, the elastic fibres also reach their maximum development, encroaching upon the connective-tissue elements until the latter become quite inconspicuous. Besides its principal transverse layer, the media also contains fusiform muscle-cells, placed in an oblique or longitudinal direction.

They are scattered irregularly throughout the middle coat. Sometimes the intima and the adventitia also contain sparsely distributed muscle-cells. The arterial muscular coat is distinctly separated from the intima by the interposition of the internal elastic coat. Externally a sharp boundary is formed either by the adventitia or by the *external elastic coat.* The latter appears as a separate membrane in arteries of small and medium size. There are, however, exceptions to this rule. The external elastic coat consists of a close network of delicate

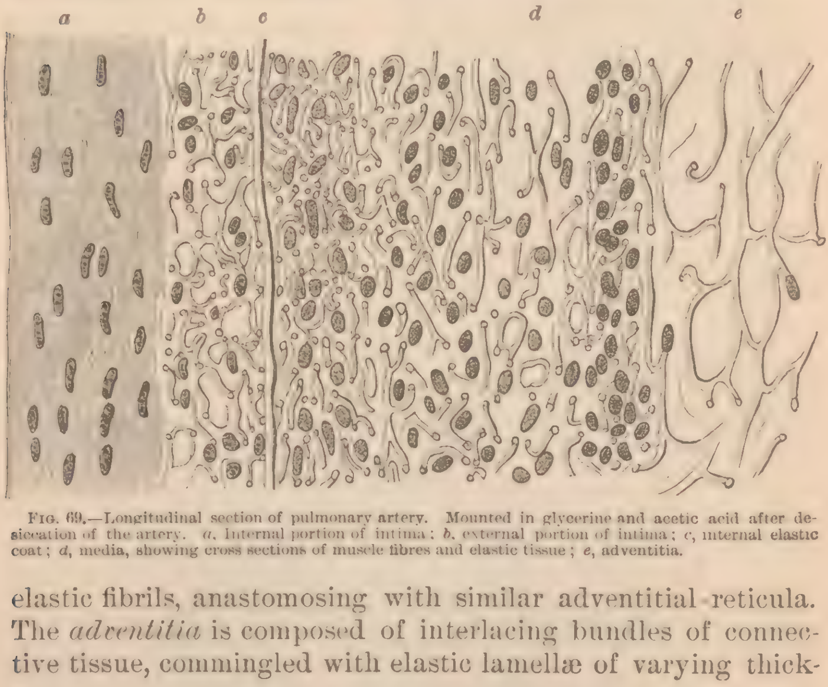

FIG. 69.—Longitudinal section of pulmonary artery. Mounted in glycerine and acetic acid after desiccation of the artery. *a*, Internal portion of intima; *b*, external portion of intima; *c*, internal elastic coat; *d*, media, showing cross sections of muscle fibres and elastic tissue; *e*, adventitia.

elastic fibrils, anastomosing with similar adventitial reticula. The *adventitia* is composed of interlacing bundles of connective tissue, commingled with elastic lamellæ of varying thickness.

The veins.—From their origin in the capillaries to the point where they enter the trunk proper, the veins preserve throughout a uniform type of structure. But no sooner have they penetrated into the visceral cavities of the body than we find them undergoing considerable alterations, which may either increase or diminish the complexity of their structure (Ranvier). The veins are far more numerous than the arteries. They are also, as a rule, wider and more dilatable, and have thinner coats. It is owing to the latter peculiarity that the

color of the blood is seen through their semitranslucent walls. Finally, they branch more frequently than the arteries. Three main coats or tunics enter into the composition of most veins. These resemble the corresponding arterial structures, and have likewise received the names of *intima*, for the internal endothelial lining; *media*, for the middle muscular; and *adventitia*, for the external connective-tissue coat.

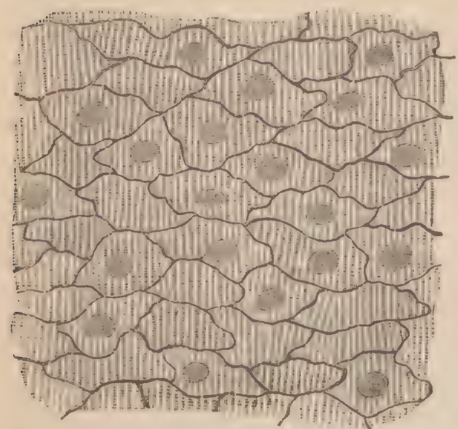

FIG. 70.—Portion of innominate vein of dog, after injection of a solution of silver nitrate. The endothelial cells and their nuclei are visible. The media shines through this layer.

Veins, however, differ from arteries in the feebler development of their muscular coat, in the comparative paucity of elastic elements, a greater laxity of their intima, and the presence in some of valves.

We may distinguish veins of smaller calibre, or *venules*, from the vessels of medium and large size. The venules, like the arterioles, in certain respects resemble the capillaries. As

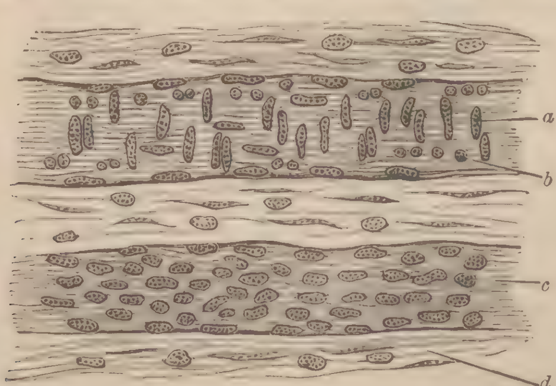

FIG. 71.—Arteriole and venule from child's mesentery, treatment by acetic acid and glycerine: A, artery; *a*, nucleus of muscle-cell of media; *b*, same in transverse section (optical). B, vein; *c*, nucleus of connective tissue constituting media, which in these minute veins contains no muscle-cells; *d*, nucleated connective tissue.

it may become important to differentiate the minuter forms of vessels, we will here briefly indicate the main points of distinction between full-sized capillaries, small veins, and arte-

rioles. In the latter, the endothelial cells are more nearly fusiform, longer, and somewhat narrower than in the venules. In the capillaries, their form and dimensions hold an intermediate position between the arterial and venous types. The middle coat is entirely wanting in capillaries, and is much less conspicuous in the small veins than in the arterioles. In fact, under ordinary circumstances, the muscle-coat forms by far the most characteristic distinguishing feature between these vessels. Venules quite frequently have only a few sparsely scattered muscle-cells, in place of the continuous muscular layer which exists in minute arteries. The former also are either altogether deficient in the internal elastic coat, or the presence of this structure is barely indicated by delicate elastic fibres; these latter usually have a longitudinal direction. On the other hand, arteries of corresponding calibre are mostly furnished with a distinct elastic inner coat. Finally, with regard to the adventitia, we find it more highly developed proportionally in venous than in arterial vessels, whereas capillaries commonly have only a few faint fibres to denote the presence, in them also, of this coat.

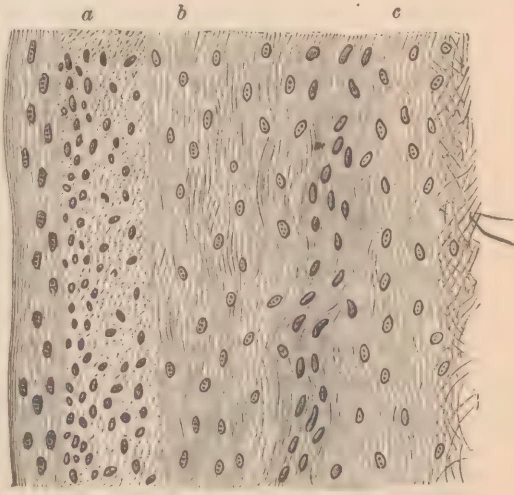

FIG. 72.—Longitudinal section of popliteal vein: *a*, intima; *b*, media; *c*, adventitia.

The *internal elastic coat* of the larger and largest veins is very feebly developed in comparison with that of the arteries. Distinct fenestrated membranes are scarcely ever encountered. Veins are likewise possessed of an *internal fibrous layer*, but here again we observe that comparatively feeble development of a coat which in the arteries is quite conspicuous.

Among the many special characteristics of the various veins in different regions, we will only mention the following: the jugular veins show well-marked elastic reticula, the meshes of which contain sparse muscular elements. In the femoral,

brachial, and subcutaneous branches there is a media of considerable dimensions. The inferior vena cava has, in addition to a transverse layer of muscle-cells, a longitudinal one of greater thickness, and, besides these, contains muscle-cells, which are scattered through its elastic coat. The veins of the meninges of the encephalon and cord, the retina, the bones, and the muscles, and the jugular, the subclavian, the innominate, and the thoracic portion of the vena cava are all entirely devoid of a true muscular coat. The veins of the gravid uterus have only longitudinal muscle-elements. In addition to an outer longitudinal layer, the vena cava, the azygos, the renal, the hepatic, the internal spermatic, and the axillary veins possess an inner circular layer. The iliac, the femoral, the popliteal, and several other veins contain a middle coat of transverse muscle-cells, between internal and external longitudinal layers.

The *valves* of the veins consist of longitudinal bundles of connective tissue commingled with scanty elastic fibrils, and containing nucleated cells. The inner endothelial layer appears to be a direct continuation of the intima of the vein. That portion of the subendothelial tissue which does not face the blood-current is less developed than the part turned toward it; the elastic fibres of the latter are also barely visible. The attached valvular border frequently presents transversely disposed muscle-elements. Eberth has denied their occurrence, but they have been repeatedly observed by Ranvier and other competent histologists.

Peculiar vascular structures.—The following structures are remarkable for the conspicuous and characteristic development of their blood-vessels the *vascular membranes*, *tunicæ vasculosæ*, such as the pia mater of the brain and spinal cord, and the choroid coat of the eye. In these we find that the excessive vascularity is intended to nourish, not the membranes themselves, but the organs which they invest.

Blood-vascular glands, vascular plexuses.—In man, two bodies of peculiar structure represent this group. They are the *coccygeal gland* of Luschka, and a rudimentary organ called the *intercarotid gland.* Both consist essentially of convoluted blood-vessels and nerves, imbedded in a nucleated connective-tissue stroma. The *coccygeal gland* is a small, rounded, pinkish body, of rather firm consistence, and is connected by a pedicle with the middle sacral artery. This pedicle contains

blood-vessels and nerves. The arteries entering the gland-like body become convoluted, and show numerous tubular, fusiform, or ampullar dilatations. Sometimes they have terminal sacculi, closely resembling minute aneurisms, and giving the organ its glandular appearance. Indeed, Luschka has called them gland-tubules and vesicles. After death they are com-

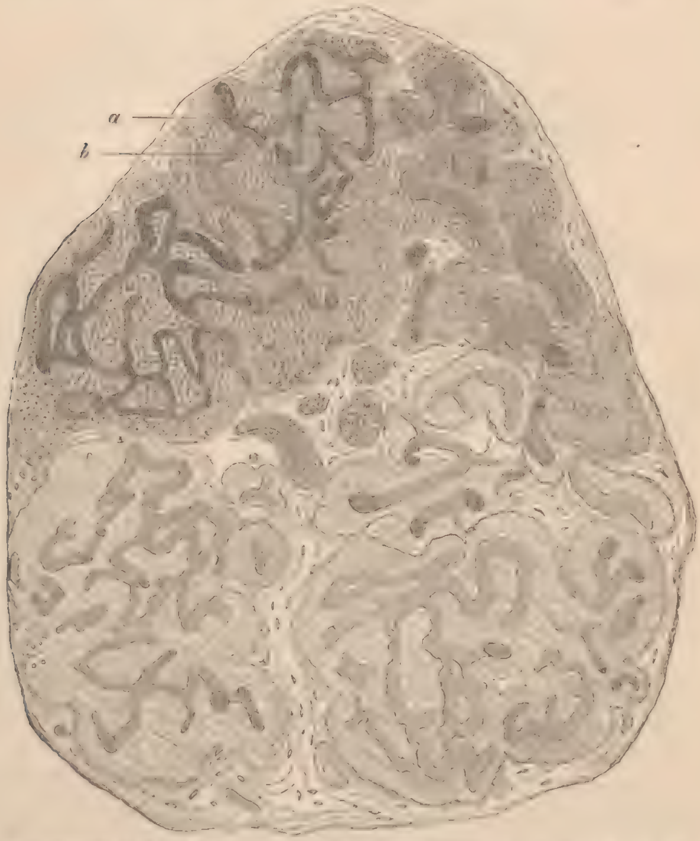

FIG. 73.—Section of a naturally injected coccygeal gland : *a*, vessels ; *b*, collection of cells. Eberth.

monly found to be empty, but by proper management a good natural injection with blood may be readily obtained. Both capillaries and veins also present lateral varicosities, studding them in great number. All these vessels have the usual endothelial lining. External to this there appear aggregations of rounded or polygonal cells. They are furnished with nuclei, and receive an investment corresponding to the vascular ad-

ventitia, but containing comparatively more nuclei than that structure.

The *intercarotid gland* differs from the coccygeal in its larger size, and because it contains accumulations of ganglionic nerve-cells. These are derived from the carotid plexus. Here the vascular sacculi also more nearly resemble dilated capillaries, whereas in the other body they approach the arterial type. In all other respects the structure of these vascular plexuses is identical. Some authors regard the spleen and the suprarenal capsule as belonging to this group of blood-vascular glands. The author sees no necessity for so considering them, and the subject may therefore be dismissed without further comment.

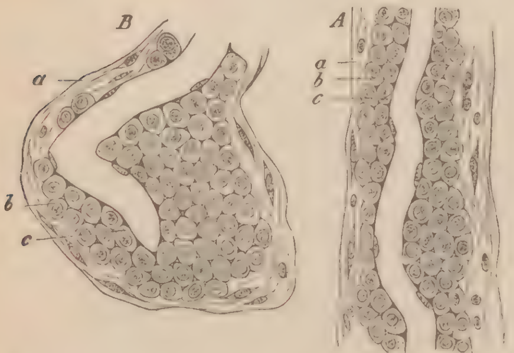

FIG. 74.—A, cellular vascular sheath, from the coccygeal plexus: *a*, connective tissue with scattered cells and nuclei; *b*, round and polygonal cells lying immediately upon the capillary wall, *c*; B, a capillary from the coccygeal plexus, with a vascular sheath very rich in cells. References as in A. Eberth.

Corpora cavernosa.—They consist in great part of dilated blood-vessels, chiefly of the venous type. These intercommunicate very freely, and when filled with blood cause the organ to assume the peculiar condition known as *erection*. The penis and the clitoris are supplied with cavernous bodies. The urethra of the female and the vestibule also contain them. Interlacing bundles of muscle-fibres, together with similar bands of connective tissue, form a framework for the support of the vascular structures mentioned. The latter present the ordinary endothelial lining.

Several years ago Dr. H. J. Bigelow succeeded in demonstrating the existence of cavernous tissue in the nasal fossæ. In a letter to the author, Dr. Bigelow states that his point was "the demonstration of an abundant and true cavernous structure and erectile tissue on and about the turbinated bones, occupying the place of what had been previously supposed to be only venous sinuses, the *loops* of Kohlrausch. The new result obtained was due to a different mode of preparation. Kohl-

rausch injected from the jugular vein; I [Dr. Bigelow] inflated the tissue locally, as if it were in the penis."

Vasa vasorum, lymphatics, and nerves.—Nutrient vessels are found in the walls of all the larger arteries and veins, where they occupy the adventitia. Sometimes they are seen to dip down into the outermost portions of the media. *Lymphatics* occur as clefts or spaces between the various tissues of all arterial and venous trunks. Some vessels are ensheathed by a lymphatic membrane, which is sometimes furnished with a lining endothelium. Such structures are called *perivascular*, or, better, *circumvascular spaces.* They may be found in connection with the omental and the mesenteric vessels, also the splenic and the hepatic arteries, as well as certain meningeal vessels of the brain and cord.

Nerve-fibres are seen to pass to many of the blood-vessels. They enter the adventitia, and at its internal boundary suddenly appear to divide into numerous filaments, the ultimate distribution of which has not hitherto been satisfactorily ascertained. They seem to terminate in the muscle-cells of the media. Beale considers the presence of ganglion-cells in the vascular nerves as of constant occurrence. The author cannot admit the truth of this general statement, having discovered such cells in only exceptional instances. There is no discernible difference of structure between the vaso-constrictor and the vaso-dilator nerve-fibres.

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CHAPTER XXIV.

THE ALIMENTARY CANAL.

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The human alimentary canal is a tube of great length, extending from the mouth to the anus. There are considerable variations of its calibre in the different regions of the body through which it passes. The two external openings of the digestive tract are continuous with the cutaneous surface of the body. Throughout its entire extent we find several superimposed layers or membranes, which are from within outward: 1, a mucous membrane with its submucosa; 2, the muscular coat; and 3, a fibrous layer. In addition to these fundamental strata, we encounter certain special structures, which characterize the various parts of the canal. The buccal cavity and pharynx are elsewhere described; we begin, therefore, with a consideration of

THE ŒSOPHAGUS.

The walls of this section of the tract are directly continuous with those of the pharynx, and have an average thickness of from three to four millimetres. In the œsophagus, in addition to the four pharyngeal coats, a new layer appears between the epithelial stratum and the submucous tissue. This new structure has received the name of muscularis mucosæ. Hence, the different layers of the œsophagus are from within outward:

1. The mucous membrane.
2. The muscularis mucosæ
3. A submucous layer.
4. The muscular coat.
5. A fibrous envelope.

The *mucous membrane* presents comparatively long, coni-

cal papillæ of more or less dense connective tissue, containing looped blood-vessels, and lined throughout by stratified pavement-epithelium. These papillæ attain a marked degree of development in the adult only. In infancy their future presence is indicated by a wavy outline at the internal attached border of the epithelial stratum. This latter portion of the mucous membrane contributes 0.22—0.26 mm. toward the entire œsophageal thickness of about 4.0 millimetres.

FIG. 164.—Transverse section through the lower part of the œsophagus of the newly-born child: *a*, *a*, epithelium; *b*, mucosa; *c*, muscularis mucosæ; *d*, submucous tissue; *e*, layer of circular muscular fibres; *f*, longitudinal muscular layer; *g*, external fibrous layer; *h*, *h*, two of the ganglia of Auerbach. Klein.

The *muscularis mucosæ* consists chiefly of longitudinal, unstriped muscle-cells. They are disposed in bundles of different sizes, separated by varying amounts of connective tissue. Toward the inferior portion of the œsophagus these bundles approach each other, displacing the interposed tissue, and forming finally one continuous muscular layer. The thickness of this layer varies between 0.2 and 0.3 mm.

The *submucous layer* is made up of fasciculated connective tissue and elastic fibres. It contains groups of fat-cells, and lodges the mucous glands. The latter closely resemble the glands found in the mouth. They consist of pyramidal or polygonal secreting-cells with conspicuous rounded nuclei, and ducts lined by cylindrical epithelia. The lower portion of the œsophagus contains smaller and more superficial acinous glands. In this region they are also found in greater abundance, and around the cardiac orifice they form almost a complete ring.

The *muscular coat* has an inner circular and an outer longitudinal layer. In man it is formed of both varieties of muscle-cells, the striped and unstriped. The upper portion is composed of striped muscle only, whereas the lower half consists exclusively of the unstriped variety. Below the upper one-eighth of the œsophagus smooth muscle-cells first begin to be blended with the other variety; they rapidly increase as we proceed

downward, until at about the middle of its course the striped fibres entirely disappear, being replaced by continuous layers of unstriped muscle-cells.

The *fibrous envelope* consists of connective tissue and elastic fibres, arranged so as to form a thin, peripheral, sheath-like membrane.

Blood-vessels and *lymphatics* are found in less abundance in the œsophagus than in the mouth and pharynx. The former are arranged in the shape of capillary networks in the mucosa. The papillary loops, already mentioned, take their origin from these reticula. The larger branches are found in the submucosa. The lymphatics occur as plexuses; one is situated superficially in the mucous membrane, and communicates by capillary vessels, with a second larger one, placed in the submucosa. The glands are said to have special lymphatics.

Nerves.—An elaborate account of the mode of distribution of nerves in the œsophagus is given in Ranvier's "Leçons d'anatomie générale," 1880, p. 366 et seq. The following brief summary gives the main points: Nervous filaments proceeding from the pneumogastrics find their way to the striped muscles, where they terminate in the well-known eminences ordinarily found in that tissue. These terminal bodies are seen to be very numerous, a fact which corresponds to the importance and complexity of nervous action concerned in the process of deglutition. The terminal distribution in the unstriped muscle presents no striking peculiarity. Between the two layers of the muscle-coat we find an arrangement analogous to Auerbach's ganglionic plexus, but the ganglia and their nerve-cells are larger and appear to be more numerous than in the intestine. The nerve-fibres proceeding from the vagus are medullated; those from the ganglionic plexus belong of course to the non-medullated variety.

THE STOMACH.

The *serous covering* of this organ has the same general structure as all visceral peritoneum, being composed of a connective-tissue membrane lined by flat endothelial cells.

The *muscular coat* of the stomach is divisible into three layers, composed of, 1, external longitudinal fibres; 2, middle circular; and 3, internal oblique fibres. All of these belong

exclusively to the unstriped variety of muscle-cells. A thickening of the inner circular layer constitutes the pyloric sphincter.

The *submucous layer* is composed of loose connective tissue, and it is for this reason that the mucous membrane is so freely movable over the muscular coat. It is, moreover, owing to this peculiarity that, whenever and wherever muscular contraction takes place, the mucous membrane presents numerous folds, ridges, and elevations. Thus, we may find in a perfectly healthy stomach appearances quite analogous to those described by pathologists as the so-called *état mamelonné* of gastritis.

FIG. 165.—Transverse section through the fundus of the stomach in a child: *a*, *a*, cylindrical epithelium; *b*, *b*, peptic tubes; *c*, *c*, muscularis mucosæ; *d*, *d*, submucous tissue; *e*, circular muscular layer; *f*, longitudinal muscular layer; *g*, peritoneum; *h*, *h*, ganglion of Auerbach. Klein.

The *muscularis mucosæ* frequently presents two layers of unstriped muscle-cells—an outer longitudinal and an inner circular one. In some regions we observe only one layer of longitudinal muscle-cells.

The *gastric mucous membrane* is covered by a single layer of columnar epithelium, containing goblet-cells in greater or less abundance. These goblet-cells represent ordinary epithelia, which appear to be bulged out by mucoid contents. At the cardiac extremity of the stomach there is a sharp, serrated line of demarcation between the œsophageal and gastric epithelial lining. The surface-epithelium forms one continuous stratum, and is continued down into the ducts of the gastric glands. The latter occur in two distinct varieties, viz., peptic glands and pyloric glands.

The *peptic glands*, also called gastric glands, are cylindrical

tubules, nearly straight or slightly tortuous, with often a single rounded cæcal extremity. However, the latter is sometimes double by dichotomous division, or we find many such blind terminal branches. Hence, we may speak of *simple* peptic glands and *compound* peptic glands. They are all placed vertically to the surface, and consist of a homogeneous basement-membrane with a lining of secreting epithelia. (Fig. 166.) The basement-membrane contains flattened nuclei, and at its inner aspect it is furnished with flat, branching adventitial cells. Each gland is divisible into a duct and gland proper. The latter, again, consists of a neck, body, and fundus.

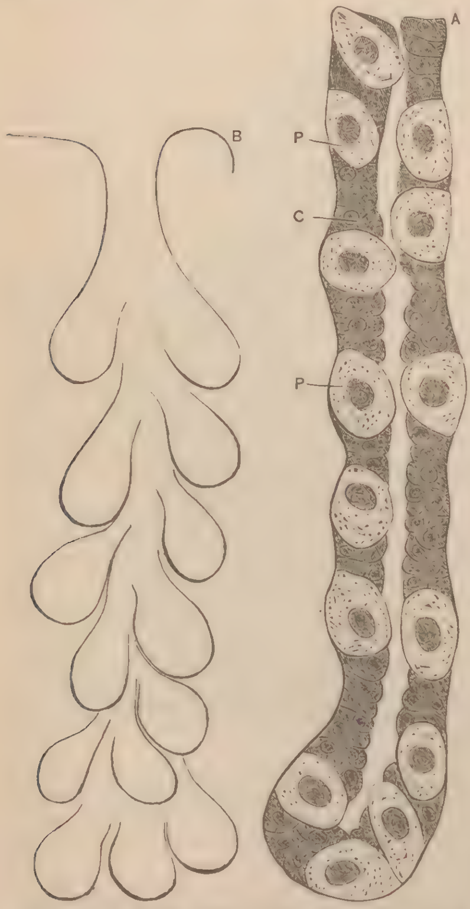

FIG. 166.—A, simple gastric gland: P, parietal; and C, chief cells. B, compound gastric gland. Only the outline, denoting the membrana propria, is drawn.

Usually, two, three, or even more of these glands, have a common duct. The length of the entire structure varies in the different gastric regions from 0.4—2.0 mm., in accordance with the thickness of the entire mucous membrane in the respective parts. The duct, amounting to about one-fourth of the whole length of the tube, is lined with one continuous layer of columnar epithelial cells, similar to the surface epithelium of the rest of the stomach. The neck, the thinnest portion of the minute tube, has similar cells; but they appear shorter, darker, and have a smaller ovoid nucleus. As regards its breadth, the body stands about midway between

the neck and the fundus, which latter is the thickest portion of the entire gland. In the neck we also find, in addition to the cells already described, other corpuscles placed externally to the former. They are the parietal cells (Heidenhain), or delomorphous cells (Rollett), the former variety being termed chief cells (Heidenhain), or adelomorphous cells (Rollett), or simply peptic cells. The parietal cells occur as spheroidal, oval, or polygonal, rather opaque, sometimes very granular bodies, which lie beneath the basement-membrane, but commonly outside the layer of ordinary chief cells. In the body of the gland-tube we again meet with these two forms of lining-corpuscles. Here, however, the columnar or chief cells are longer than in the neck, and their bodies generally appear more transparent, while the nuclei, again spheroidal, are situated nearer the external than the internal border. Klein describes the substance of these cells as consisting of a delicate reticulum, with a small amount of a hyaline interstitial substance in its meshes. The same author, also, invariably finds an intra-nuclear network. Others have been less fortunate in finding such appearances. The parietal cells of the body in all respects resemble those of the neck. As the fundus is approached their number grows comparatively less.

The *pyloric glands*, which some histologists insist on calling mucous glands, are lined throughout by a single layer of epithelium. This is composed of the ordinary columnar cells of the gastric surface. But the corpuscles here appear to be somewhat compressed, so that they seem less transparent than elsewhere. They are known to undergo certain changes during their passage from activity to rest. Examined in the latter condition, we find them more granular, and apparently smaller or shorter, than during and immediately after secretion. These glands have long ducts, each one serving for several secreting tubules. Their bodies are branched, and usually appear somewhat tortuous. When such glandules become somewhat more complex and grow larger (a change which normally takes place in the duodenum), they are called Brunner's glands.

Dr. Edinger has recently (*Archiv f. mikr. Anat.*, Vol. XVII., p. 193) asserted that the gastric glands contain in reality only one kind of cellular element. He based his opinion on results obtained by treating the almost living mu-

cous membrane with osmic acid, after Nussbaum's method. By him the chief cells are said to develop into parietal cells, through an increase of their volume and a filling up with the gastric ferment. The considerations which led him to form this opinion are as follows: 1, the occurrence of bodies which represent transition-forms between chief cells and parietal cells; 2, the analogy of this assumed metamorphosis of gastric corpuscles (*i.e.*, the conversion of chief cells into parietal cells), with similar changes, known to occur in other glands during active secretion; 3, the fact that many animals which secrete pepsin have only the parietal cells; 4, the results of an examination of the mucous membrane of starving animals, which revealed only the chief-cell form of gastric corpuscles; and 5, the apparent discrepancy in the descriptions of these bodies by competent histologists—some observers regarding the chief cells, others the parietal cells, as exclusively pepsinogenous.

Still more recently, Stöhr has (*Verhandl. d. phys.-med. Gesel. in Würzburg*, 1881, p. 101) studied the histology of the gastric epithelium. His specimens were derived from the fresh stomach of a criminal immediately after execution of the latter. The man had taken no nourishment for some hours before his death. The principal conclusions of Stöhr are: 1, the epithelia of the mucous glandules are not destroyed during the process of secretion, but, like those of the true gastric glands, continue their existence; 2, the parietal groups of cells represent those portions of the mucous corpuscles which have not undergone mucoid metamorphosis, being made up of unaltered protoplasm.

From the above contradictory statements it appears that even to-day our intimate knowledge of the gastric mucous membrane, and especially its epithelia, is far from being in a satisfactory condition. It will have to be reserved for future investigations to dispel the uncertainty still existing with regard to some of the most interesting details of the physiologico-histological characteristics of the inner coat of the stomach.

The *blood-vessels* of the stomach have an arrangement similar to that of the œsophagus. In the mucous membrane, however, we find abundant plexuses of capillary vessels surrounding the gastric glands. These networks intercommunicate, and just beneath the surface-epithelium they become especially

close. From this point the veins take their origin. The venous rootlets unite in a stellate manner to form larger branches, which descend almost vertically and empty into a venous reticulum situated between the glandular layer and the muscularis mucosæ, and just above a similar arterial network.

Lymphatics abound in the stomach. They appear to arise from superficial loops, which, anastomosing between the

FIG. 167.—Lymphatics of the gastric mucous membrane of the human adult. Frey.

glandular tubules, reach the fundal zone of these structures. There they form a network, and this is in communication with a plexus of larger vessels, situated in the submucous tissue.

The distribution of the *gastric nerves* does not differ materially from that of the small intestine, in the description of which this matter will receive more particular attention. Ganglion-cells are frequently found both in the muscular layer and the submucosa; in the latter we have a tolerably distinct plexus of nerve-filaments and ganglion-cells.

Of the normal occurrence in the walls of the stomach, of true lymphoid follicles, the author has been unable to find convincing evidence. Nevertheless some writers assert that they are always to be found there.

THE SMALL INTESTINE.

The *serous coat* presents no structural characteristics peculiar to itself, closely resembling the gastric peritoneum. It encloses a muscular coat and the mucous membrane, which are held together by connective tissue. The average thickness of these layers does not, in man, exceed 1.0 mm., of which three-fourths belong to the muscular, and one-fourth to the

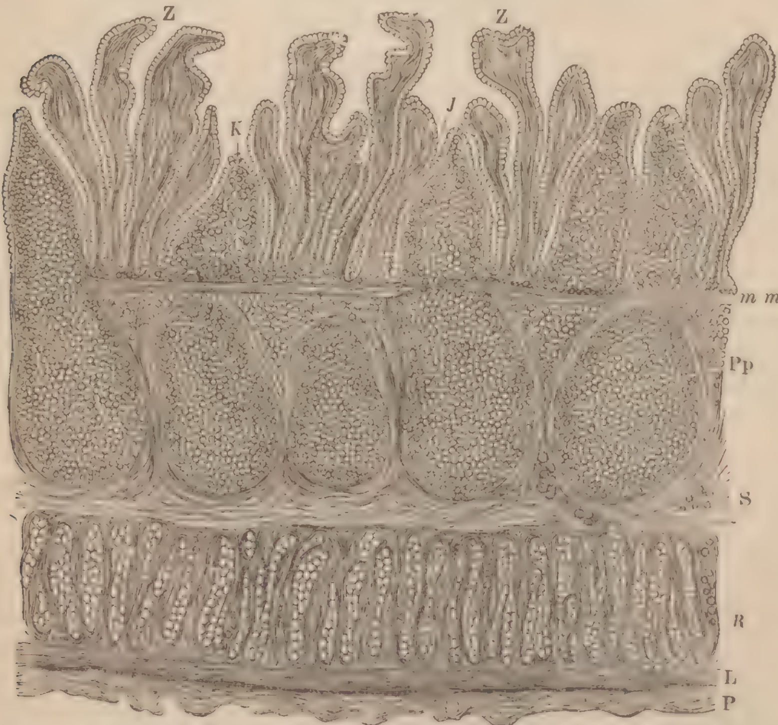

FIG. 168.—Longitudinal section of the small intestine of a rabbit: Z, Z, villi; J, crypts; Pp, a Peyer's patch; K, cap of a follicle; S, submucosa; *m, m*, muscularis mucosæ; R, circular muscular layer; L, longitudinal muscular layer; P, peritoneum. Verson.

mucous coat. Of course, the contracted or relaxed condition of the intestinal tube at the time of measurement will appreciably influence these figures. But they represent the general ordinary average.

The *muscular coat* has an external longitudinal and an internal circular layer. Between the two we find Auerbach's

plexus myentericus of flat nerve-fibres, which will be described farther on. The muscle-coat becomes gradually thinner as we pass from the duodenum to the ileo-cæcal valve. In the formation of this thickened fold the longitudinal layer does not participate.

The unstriped muscle-cells have an average length of 0.255 mm., and are about 0.005 mm. broad. They are arranged in bundles, surrounded by connective-tissue bands, with which elastic elements are abundantly interwoven.

The *mucous membrane* is thrown into folds, and is studded with closely placed projections, called villi. The general direction of these folds, the *valvulæ conniventes Kerkringii*, is parallel to the transverse course of the circular muscle-layer. They run parallel to one another, or join at acute angles.

The *villi* jut out into the lumen of the intestinal canal, as variously shaped projections, of an average length of 0.04—0.6 mm., and an average breadth of 0.06—0.12 mm. In general their form may be said to be conical or cylindrical; but we always encounter a great variety of shapes, in accordance with the varying states of contraction in the muscularis mucosæ. Each villus consists of a large-meshed reticulum of connective tissue, infiltrated, as it were, with leucocytes, and containing flattened corpuscles, which resemble endothelial cells. One or several spaces, situated in the centre of every villus, constitute the origin of the lacteal tubes. According to Brücke, these chyle-vessels are covered by thin, but not continuous bundles of smooth muscle-fibres. Their walls show only a single layer of ordinary endothelial cells, with clear oval nuclei. The free surface of the villi, like that of the stomach, is covered by a single layer of columnar epithelium. Each cell presents, in the recent state, a finely striated hyaline band at its unattached border. This structure has, at different times, received various interpretations, and even now opinions

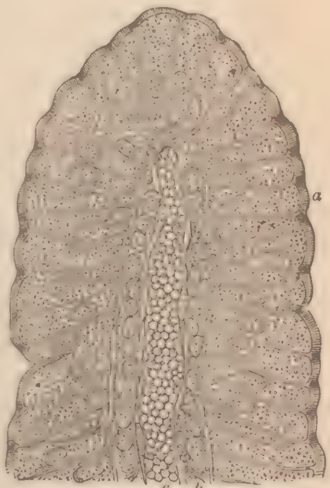

FIG. 169.—Section of a villus from the intestine of a rabbit: *a*, epithelium; *b*, stroma; *c*, central cavity. Verson.

are much divided as to its true significance. Some histologists regard the striæ as indicating so many minute pores for purposes of absorptive transmission; others believe that the juxtaposition of numerous delicate rods explains the peculiar appearance; and Klein has lately asserted them to be merely prolongations of the fibrils of the cell-substance composing the epithelia. These striæ are always seen to run parallel to the long axis of the cells.

Krause also described as of normal occurrence, a basal process extending at an obtuse angle from the attached surface of these bodies, and inserted into the delicately serrated border of the villi. Near its attached border each epithelium presents a bright ovoid nucleus, with one or more distinct nucleoli. Besides the ordinary corpuscles, we find interposed between them the so-called goblet-cells. These are derived from the former by mucoid infiltration of the cell-body, which is therefore conspicuously bulged out. Lymph-corpuscles also occur between the epithelia.

Immediately beneath this layer we find a delicate, homogeneous *basement-membrane*, composed of flattened cells, resembling endothelia.

The *muscularis mucosæ*, or muscle of Brücke, is made up of a single or double layer of smooth muscle-cells. When double, an inner circular may be distinguished from an external longitudinal coat, both being always very attenuated.

The *submucous layer* is formed of connective tissue, the supporting framework of which contains lymphatics, blood-vessels, nerves, and often groups of fat-cells.

The *glands of the small intestine* are those of Brunner and the crypts of Lieberkühn. In addition to these, however, there occur numerous lymphoid follicles, which, when found singly, are known as the *solitary follicles*, and, when grouped together, as agminated glands, or *Peyer's patches*. The solitary or closed follicles are real lymphoid glands, and, like these, consist of reticulated connective tissue, the meshes of which are replete with lymph-corpuscles. The jejunum, ileum, and colon all contain such follicles, but the agminated glands occur in the ileum, abounding especially at its lower part. Around each follicle we find a ring of villi and glands, which arrangement goes by the name of *corona tubulorum* (Müller). The follicles receive an enveloping layer of fibro-connective tissue.

Brunner's glands lie in the submucosa, where they form closely crowded tubules, separated by a small amount of connective tissue. Smooth muscle-cells, starting from the muscularis mucosæ, are often seen to pass between them. These convoluted tubules resemble and correspond to the gastric glands, but have here attained a much greater degree of development.

FIG. 170.—Vertical section through a human Peyer's patch, with its lymphatics injected: *a*, intestinal villi with their lacteals; *b*, Lieberkühnian glands; *c*, muscular layer of the mucous membrane; *d*, apex of the follicle; *e*, middle zone of the follicle; *f*, basis portion of the follicle; *g*, continuation of the lacteals of the intestinal villi into the mucous membrane proper; *h*, reticular expansion of the lymphatics in the middle zone; *i*, their course at the base of the follicle; *k*, continuation into the lymphatics of the submucous tissue; *l*, follicular tissue in the latter. Frey.

They also appear to have been pushed down, as it were, from the mucous into the submucous layer.

An individual gland consists of its long duct lined by columnar epithelium, and the branched tubules, which frequently have terminal clusters, resembling true acini. They are, however, only secondary or tertiary diverticula, so that Brunner's glands really conform to the compound tubular type of secreting structures (Renaut). Each ultimate diverticulum has an external membrana propria composed of flattened endothelial cells, and a lining of cylindrical, columnar, or prismatic secreting epithelia, containing oval nuclei.

Histologists have described minute capillary channels proceeding from the central lumen of the gland, between the secreting-cells, ending just underneath the membrana propria. The author believes these intercellular channels, as they have

been called, to be the artificially altered cement-substance always present between such adjacent cells. Brunner's glands abound only in the duodenum, but a few may occasionally be seen lower down the intestine. Their ducts, after traversing the muscularis mucosæ, ascend almost vertically between the crypts, opening on the free surface of the mucous membrane.

Fig. 171.—Crypts and interfollicular connective tissue, from the intestine of the rabbit: K, crypt; *a*, *a*, epithelium; *d*, adenoid tissue, from which the cells have been removed by pencilling; T, fibrous tissue on the opposite side. Verson.

These crypts represent open spaces within the so-called *follicles of Lieberkühn*, which are tubular glands placed vertically in the intestinal mucous membrane, existing throughout its entire extent.

They form a continuous layer, except where the upward projection of a lymph-follicle creates an interruption. These glands open at the base of the villi, the epithelial covering of the latter being continued down into the tubular depressions which they constitute in the mucous membrane. The cells of this stratum naturally appear broader at their attached than at

their free extremities. A continuation of the villous basement-membrane forms the membrana propria of the crypts of Lieberkühn. External to this we find the surrounding connective tissue, which is disposed in reticula, containing many leucocytes in its meshes. Hence it is also known as adenoid tissue.

The *blood-vessels* enter and leave the intestine at the mesenteric margin. The arteries, generally accompanied by one or two veins, pierce the muscle-coat, giving off branches which form networks in those layers, then enter the submucosa, where they run parallel to the surface of the mucous membrane, and finally send off vertical arterioles at the base of the villi. The latter ascend on one side of the villus, and then suddenly divide into a dense capillary network. This division takes place near the middle, the capillaries then spreading out to the apex and periphery. Here they become quite superficial, being covered by the epithelial lining only. The venous rootlets of the villus are generally two, or even three in number. About the glands and follicles we encounter special networks with variously shaped meshes.

Lymphatics are found in all the layers of the intestinal canal. Those of the serous coat empty into the large mesenteric trunks. In an inward direction we also find a network of lymph-capillaries between the two layers of the muscle-coat. The submucous layer contains the perifollicular lymph-sinuses situated at the base of these bodies, and a reticulum of larger channels, many of which are found provided with valves. The lymphatics of the mucous membrane are present in the shape of capillary networks surrounding the intestinal glands.

In the villi we note, as already stated, one or more central lacteals, communicating at the base of these structures with the lymph-vascular networks situated around and between the glands.

The *nerves* of the intestine are known as the *plexus of Auerbach*, and of *Meissner*. The former, situated between the circular and longitudinal fibres of the musculosa, is composed of flattened nerve-branches, made up of numerous ultimate fibrils. Small nodules, containing characteristic ganglion-cells, are also found, while little twigs are given off from the plexus myentericus, to be distributed to the layers of the musculosa.

The *plexus of Meissner* is situated in the submucous tis-

sue. Its component nerves are less flattened, but are likewise provided with ganglia containing variously shaped ganglion-cells. This plexus also gives origin to the secondary networks of the muscularis mucosæ, and is besides connected by certain branches with Auerbach's plexus.

THE LARGE INTESTINE.

The histological structure of the colon, broadly speaking, very nearly resembles that of the preceding section of the alimentary canal. The lining epithelium of the mucous membrane presents the same characteristic appearances as in the

FIG. 172.—Section of the large intestine of a rabbit: *J*, crypts of Lieberkühn: *a*, epithelium; *b*, mucosa; *m*, muscularis mucosæ; *s*, submucosa: *R*, circular muscular layer; *L*, longitudinal muscular layer; *p*, peritoneum. Verson.

small intestine. The mucosa of the colon is, however, devoid of villi; but it shows numerous crescentic folds. The muscularis mucosæ will be found to answer to the description already given of that layer in the small intestine.

The submucosa also shows the same morphological composition, but appears to be much richer in deposits of fat-cells. Aggregations of lymph-follicles are not generally found, but large, conspicuous solitary glands abound throughout.

The crypts of Lieberkühn are identical with the glands of

the same name found in the small intestine. As we approach the rectum an increase in their length becomes apparent.

In the *vermiform appendix* we find the collection of solitary lymph-follicles so closely placed that the space left between adjoining glands does not equal in diameter that of these structures themselves.

The longitudinal layer of the muscle-coat is quite thin between the tæniæ coli, or flat longitudinal bands of the large intestine. These bands themselves represent thickened layers of the musculosa. It appears that the circular fibres are especially developed in the portions between the sacculi of the cæcum and colon.

The *blood-vessels* are arranged after the same plan as in the small intestine. In the submucosa are contained large trunks, running parallel to the surface. Capillaries arise from these, and ascend almost vertically between the crypts of Lieberkühn, the capillary network surrounding those structures being only moderately developed.

As regards the *lymphatics*, they have a distribution similar in all essential respects to that found in the small intestine.

The *nerves* likewise imitate in their structure and arrangement those encountered in the small intestine. Meissner's plexus appears to be provided with comparatively large ganglia and relatively small component cells. The plexus of Auerbach also attains conspicuous development in the large intestine.

THE RECTUM.

The internal sphincter ani represents a thickening of the circular layer of the muscle-coat. In its upper portion the rectal mucous membrane is like the same structure of the large intestine. Lower down we find the columnar epithelium gradually replaced by stratified pavement-epithelium.

The follicles of Lieberkühn are large and long. Finally, the mucous membrane gradually passes into the ordinary integument surrounding the anal orifice.

The blood-vessels, lymphatics, and nerves resemble in their distribution those of the colon, and are devoid of characteristic peculiarities.

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would aid the contraction of the muscle. In specimens where the muscle is found in a state of contraction, the hair-follicle is bent like a bow, the root being drawn through the arc of a circle. The presence of fat near the hair-bulb is made possible by this structure, a condition which is constant with all hairs. That the fat is not an incidental feature of their structure, which might be considered merely a cleft for the transmission of vessels, is rendered probable by the observation of rows of fat-cells beneath each hair in the lip of the rat, where no special channels exist, and, also, by the fact that such columns of fat do not accompany the nutrient vessels of the skin, in those parts where the hairs are not found. It seems, therefore, probable, that this structure has some bearing upon the nutrition of the hair.

Sweat-glands are found not only in these canals, but elsewhere in the thick cutis; the coil of the gland is then usually situated at a level a little below the middle of the cutis vera, and not in the subcutaneous adipose tissue, as in thin skin.

CHAPTER XXVII.

URINARY EXCRETORY PASSAGES; SUPRARENAL CAPSULES.

By EDMUND C. WENDT, M.D., New York City,
Curator of the St. Francis Hospital, etc.

The renal pelvis, the calices, ureters, and bladder, all consist essentially of three layers, which are an inner mucous membrane, a middle muscular coat, and an external fibrous layer. In the

RENAL PELVIS

we find the *mucous membrane* lined with stratified epithelium, the cells of which are large and variously shaped. Three different forms are readily distinguished. The most superficial layer consists of flat or polyhedral cells of various sizes, each one containing a round or oval nucleus, or, as frequently happens, two nuclei. Peculiar dark granules, often of large size, surround the nucleus, and are quite distinct from the finely granular protoplasm of these cells. Then comes a layer of conical or club-shaped bodies, each one again furnished with a round or oval nucleus. Every cell also possesses a long basal process, which appears to attach it to the subjacent tissue. The bulbous portion of these corpuscles is turned outward in the direction of the surface. Wedged in between the processes just mentioned we find the third variety of cellular elements. These are oval or rounded bodies containing ellipsoid nuclei. At the renal calices we find a sharp line of demarcation between the cylindrical columnar epithelium of the papillary ducts and the stratified pavement epithelium of the pelvis. The epithelial layer has a thickness here of 0.045–0.09 mm.

The connective-tissue portion of the mucous membrane is devoid of papillæ, contains sparse elastic fibres, and is rich in

fixed corpuscles, the inoblasts of Krause. There is no true basement-membrane. Below this stratum we find a submucous layer, which is abundantly furnished with elastic tissue, and contains a few simple acinous glands with ducts having a lining of cylindrical epithelium.

The *muscular coat* is composed of bundles of smooth muscle-cells forming an inner layer, with a peripheral direction of its constituent anatomical elements, and an outer layer concentrically arranged. The "papillary sphincter" is but a thickening of this latter layer.

The *external fibrous layer* forms a thin connective-tissue membrane, not always clearly marked here, whereas in the ureters and bladder it is found to be well developed.

The *blood-vessels* of the pelvis are derived from the renal artery and vein, and form capillary networks characterized by polygonal meshes. The lymphatics and nerves are found to have the same distribution as in the ureters.

THE URETERS

have a structure which closely resembles that of the renal pelvis. The *mucous membrane* shows the same varieties of epithelium; its connective-tissue components are similarly arranged; and the external investing membrane is composed of the same kind of tissue already described. But in addition to the two *muscular layers*, which here attain a greater development, we find a third muscle coat, so that we can now distinguish an internal and external longitudinal from a middle circular layer of muscular elements.

Engelmann has described a close reticulum of blood capillaries lying immediately under the epithelial stratum, but its existence is made doubtful by the negative statements of other authors.

Glandular bodies are not found in the ureters. The peripheral layer of fibrous connective-tissue possesses conspicuous elastic bundles in the lower portion of the ureters.

The distribution of the *blood-vessels* is like that of the pelvis already described. The *lymphatics* are well developed here, forming several networks in the different layers of the ducts. *Nerves* are likewise readily distinguished, some of the nerve-

fibres being also furnished with ganglion cells. Their mode of termination in the muscular layer is not definitely known, but may be assumed to resemble that of ordinary smooth muscular-tissue.

THE BLADDER

has the same type of structure as the ureters, but contains, in addition, a serous covering in its upper portion. The different coats of the bladder are, however, much thicker than the corresponding layers in the other urinary excretory passages.

The *epithelial* lining of the mucous membrane shows the three varieties of its cellular elements in a clearly defined manner.

The *connective-tissue* stratum presents no noteworthy peculiarities, if we except the comparative abundance of simple acinous glands.

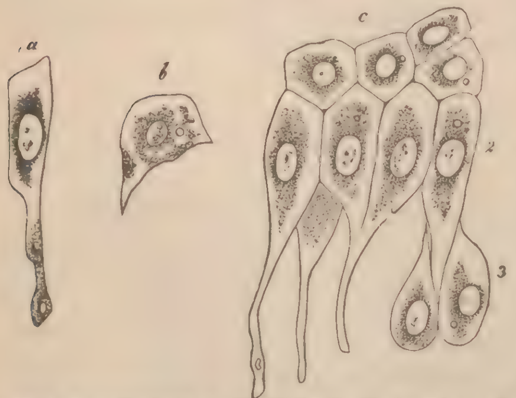

FIG. 182.—Epithelium of the urinary bladder. *a*, a cell of the second layer; *b*, a cell of the first layer; *c*, shows the first, second, and third layers of the epithelium in connection. Obersteiner.

The bundles of muscle-cells in the *muscular-coat* interlace, forming irregular, long-stretched meshes. This irregular arrangement prevents the distinct recognition of successive layers, each with a largely prevailing direction. Nevertheless, we find in the external portion of the muscle-coat some predominance of longitudinal bundles, together with an abundant supply of elastic fibres. The anterior wall and vertex of the bladder show this arrangement very conspicuously, in fact the muscle-fibres have here received a separate name, that of *detrusor urinæ*. The vesical neck shows a tolerably distinct thickening of its circular muscle-fibres, which is known as the *sphincter vesicæ*. It should always be borne in mind that the arrangement of the muscular coat is apt to vary in different individuals, the description here given will, however, be found to apply to the majority of cases.

The *blood-vessels* form a capillary network in the mucous membrane, which is situated about midway between the epithelial stratum and the muscular coat. In other respects they present no peculiarity worthy of note.

The *lymphatics* are less abundant in the bladder than in the ureters. They, also, lack noteworthy peculiarities or special features of interest.

Plexuses of *nerve-fibres* are found in the subserous connective-tissue, and also in the muscular coat. Microscopic ganglia and groups of ganglion cells are also met with.

SUPRARENAL CAPSULES.

The suprarenal capsules (*glandulæ suprarenales*) are small flattened bodies, two in number, situated somewhat above and

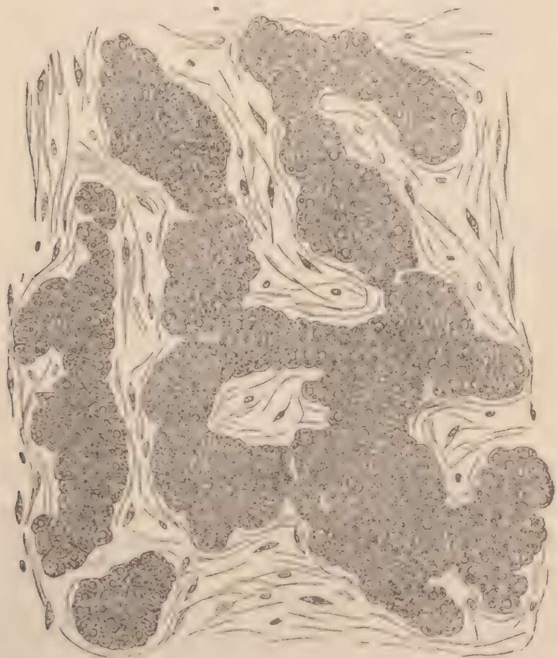

FIG. 183.—Cellular groups and trabeculæ of the cortical substance, from the suprarenal capsule of the Frog. Eberth.

in front of the upper end of either kidney. They are usually triangular or semilunar in shape, although round and oval forms are also met with. In structure they resemble the so-

called blood-vascular glands, but their function is not known. They belong to the ductless variety of glands.

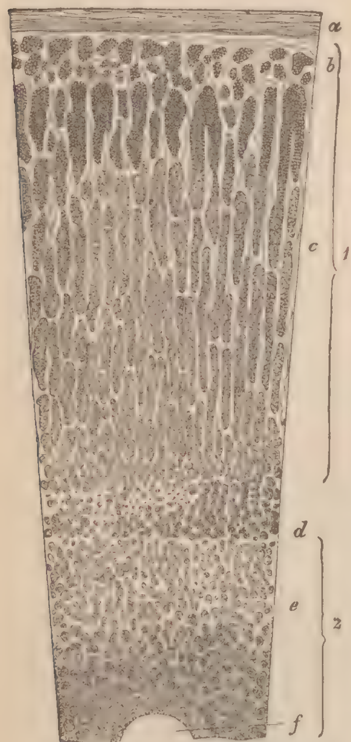

FIG. 184.—Perpendicular section through the suprarenal capsule of man: 1, cortex; 2, medulla; *a*, capsule; *b*, layer of outer cell-groups; *c*, layer of cell-trabeculæ (zona fasciculata); *d*, layer of inner cell-groups; *e*, medullary substance; *f*, transverse section of a vein. Eberth.

Each suprarenal body consists of a capsule inclosing the parenchyma, which shows a cortical and medullary substance. The *capsule* is formed of ordinary connective tissue containing many delicate elastic fibrils. Externally it is surrounded by loose connective tissue, containing a greater or less proportion of adipose tissue, and internally it sends out trabeculæ, which traverse the entire organ, thus constituting and completing its frame-work.

The *cortical substance*, as its name implies, occupies the external portion of the suprarenal body. It has an average thickness in man of 0.28 to 1.12 mm., is of a yellowish color, and may be divided into three layers or zones. The limits of demarcation between these layers are much less marked, however, than the corresponding boundary line between the cortical and medullary portions. In the human being the external layer of the cortex is distinctly separate from the middle one, but the latter shows no such sharp limit against the innermost layer. The cortex is a friable substance, and its broken surface presents a striated appearance. Owing to rapid post-mortem changes, the cortex in man is usually found to be separated from the medullary portion by a dirty brownish substance, containing modified blood and cortical corpuscles.

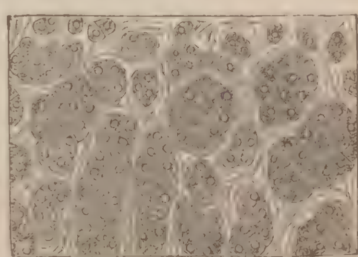

FIG. 185.—Single cells and cell-groups of the outermost cortical layer. Human suprarenal capsule. Eberth.

The three layers of the cortex are an external one, or *zona glomerulosa*; a middle one, or *zona fasciculata*; and an internal one, or *zona reticularis*.

The *external layer* consists of rounded or oval groups of cells, separated by delicate connective-tissue trabeculæ, which spring from the capsule. Similar cells are found throughout the entire cortex. They have been called the parenchymatous bodies or cells, although a better name is cortex corpuscles. In structure they resemble ordinary cells, consisting of poly-

FIG. 186.—Horizontal section through the outermost cortical portions of the suprarenal capsule of the Horse. *a*, blind termination of a cylinder; *b*, groove-shaped and cylindrical cortical trabeculæ; *c*, stroma. Eberth.

hedral masses of protoplasm furnished with spherical nuclei and conspicuous nucleoli. Their protoplasm has a coarsely granular character, and, as a rule, contains more or less fat in greater or smaller droplets.

The *middle layer* contains cortical corpuscles which are arranged in almost parallel rows, and are so closely packed that this portion acquires a distinctly striated appearance. These cellular columns have received various names. By Ecker they were called gland tubules, Kölliker termed them cortical cylin-

ders, Eberth described them as cylindrical cell-trabeculæ, or cortical trabeculæ, and Krause named them cellular pillars. These cellular rows, columns, or streaks, are by no means always cylindrical, for on cross-section they frequently present a semilunar, oval, or bean-shaped appearance. Their inner and outer terminations have a rounded shape, and near the former place they seem to anastomose with one another. At

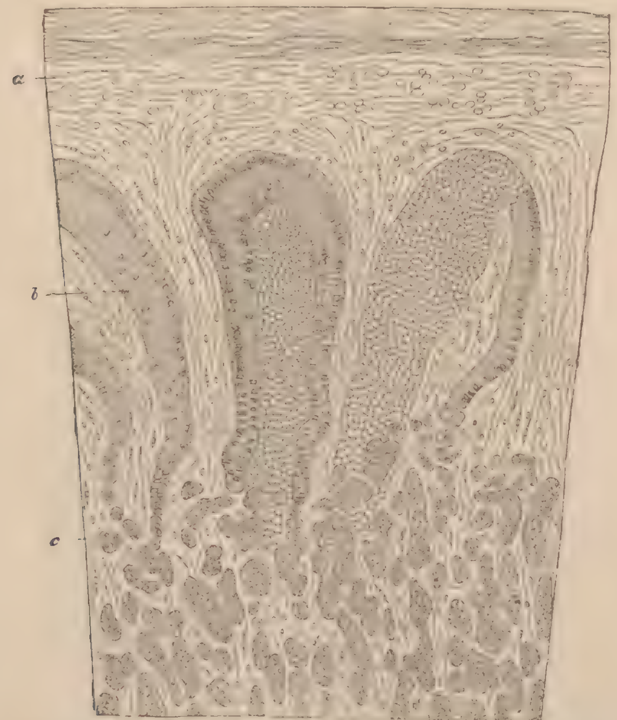

FIG. 187.—Vertical section through the the cortical portion of the suprarenal capsule of the Horse. *a*, capsule; *b*, cell-trabeculæ; *c*, cell-groups. Eberth.

the peripheral end they sometimes appear groove-shaped, or in horse-shoe form.

Connective-tissue processes communicating with the capsule are found between the cell columns, but the latter are not completely isolated by them. These connective-tissue streaks also send off transverse or oblique fibres, so that occasionally the cells of the middle layer seem to be inclosed in basket-like meshes. In addition to fat-droplets, granules of pigment are

found in the cells of the innermost portion of the middle layer.

The *external layer* is made up of irregularly arranged cortical corpuscles. Nearly all the cells of this layer contain pigment granules. The connective-tissue here forms a reticulum, with variously shaped meshes, which contain greater or smaller heaps of cells.

The *medullary substance* has a whitish-gray appearance, and is of a more delicate consistency than the cortex. It consists

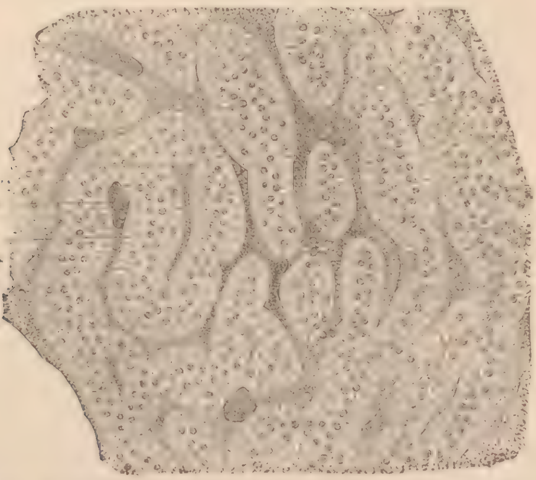

FIG. 188.—Vertical section through the medullary substance of the suprarenal capsule of the Cow. *a*, blood-vessels; *b*, trabeculæ of medullary cells. Stricker.

of a network of connective tissue, which contains in its meshes the medullary corpuscles. These are pale cells with spherical nuclei and large nucleoli. They may assume various shapes. In man they are generally of an irregularly stellate or polygonal form. Their protoplasm is finely granular, and they contain, as a rule, much less fat and pigment than the cortical corpuscles. Kölliker finds that they resemble the nerve-cells of the central nervous system, but he adds that they cannot be regarded as such nerve-elements. The medullary cells assume a yellow or brownish color when treated with chromate of potash or chromic acid. Since the cortex corpuscles are not thus colored, this peculiarity may serve to distinguish one cellular variety from the other.

The connective-tissue framework of the medulla is called its

stroma, and its meshes in man have an oval or rounded form, so that, as a rule, the cell-groups have a similar shape. On the whole, we find a smaller proportion of connective tissue in the medulla than in the cortex.

The *blood-vessels* of the suprarenal capsules occupy the stroma, and are found in great abundance. The arterial vessels arise from the aorta, the phrenic and renal arteries, and the cœliac axis. About twenty small branches pierce the capsule, and are distributed mainly to the cortex. The medullary substance is very rich in venous plexuses. Capillary networks are found in both cortical and medullary portions. The veins uniting form one principal branch, which passes out at the hilus of the organ. The right suprarenal vein empties its blood into the vena cava inferior, the left one into the vena renalis sinistra.

Lymphatics were seen by most observers only at the surface of the suprarenal capsules. Klein, however, has recently asserted that there exists between the cells "an anastomosing system of narrower and broader clefts, channels, and lacunæ, which belong to the lymphatic system." This applies to the zona fasciculata. In the other portions of the organ the same writer also finds lymph-spaces, and lymph-sinuses, occupying the regions "between the septa and trabeculæ of the framework on the one hand, and the cell-groups on the other."

The *nerves* occur in comparatively greater abundance in these organs than in any other glandular structures of the human body. Kölliker was able to count thirty-three branches in a single suprarenal capsule of a man. They are derived from the renal plexus, the pneumogastric and phrenic nerves, and semilunar ganglion. Very fine or medium-sized, dark-bordered fibres are commonly encountered, and they abound especially in the medulla. Ganglion-cells are also frequently seen, and Virchow has traced them into the interior of the organ. In the cortical substances they are of rare occurrence. The terminal distribution of the nerves has not been hitherto ascertained, and it appears to be still a matter of doubt whether they terminate in the suprarenal body at all.

Development.—In mammals the suprarenal capsule has an independent origin in a collection of tissue between the Wolffian bodies behind the mesentery and in front of the abdominal aorta. (Kölliker.) The mesoderma at this point assumes

a special structure. Certain of its cells form more or less cylindrical masses with a reticulated appearance. Between these cellular groups a network of blood-vessels is soon found, so that the whole structure is now not unlike embryonal hepatic tissue. In rabbits, Kölliker saw the first traces of these bodies about the twelfth or thirteenth day. On the sixteenth day they had already attained a length of 1.56 mm., and occupied a position along the vertebral column from the first to the fourth and part of the fifth lumbar vertebra. On cross sections of embryos sixteen days old, Kölliker found that the suprarenal capsules were distinctly separate at their upper borders, whereas their lower ends were joined together to form a single organ. The same writer also found a nervous ganglion at the coalesced central portions of somewhat older embryos.

Behind the suprarenal capsules a second sympathetic ganglion was discovered. Remak and v. Brunn do not in all respects corroborate the statements of Kölliker. The latter was unable to ascertain any existing relationship between the nervous system and the suprarenal capsules.

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CHAPTER XXVIII.

THE MAMMARY GLAND.

By W. H. PORTER, M.D., and EDMUND C. WENDT, M.D., of New York City.

General considerations.—By virtue of its intimate association with the function of reproduction, this organ occupies a distinctly peculiar position among the glands of the body. In the male it persists through life in the same rudimentary form which characterizes the mamma of both sexes at birth. Only in the female, and in her only at certain times, does this organ attain its complete histological maturity. It may be borne in mind, however, that in a few anomalous cases, male beings supplied with fully developed mammary glands have been observed.

After conception, and as pregnancy advances, progressive evolution takes place within the mamma. This unfolding process at length culminates in exaggerated tissue-metamorphosis, which in other organs we should scarcely hesitate to call pathological. In fact, Virchow and his followers all maintain that the secretion of milk is the direct result of a fatty degeneration of mammary epithelium, and similar in all essential respects to the processes involved in the elaboration of the sebaceous material from the cutaneous glands of that name. Billroth, indeed, calls the mammæ cutaneous fat-glands (*Hautfettdrüsen*), and he does this in consideration of the mode of their development, and because they are placed immediately beneath the integument. In spite of these statements, however, we must maintain that the mammæ are radically different from ordinary sebaceous glands, and that the processes of secretion in the two sets of glands are quite distinct. The grounds on which we base this opinion will be amplified farther on. The secretory activity of the gland, consisting in the elaboration of milk, is, as a rule, called into play only during the period

of rapid growth and development already alluded to. In exceptional instances, however, lacteal fluid may be secreted during the extra-puerperal period.

The mammæ belong to the class of compound acinous or racemose glands, and, like the other organs of this group, consist of a framework or stroma, and a proper secreting structure or parenchyma. As they appear to the naked eye, the bulk of the breasts is not their secreting parenchyma, but ordinary adipose tissue. This fills out the intervals between the lobes and lobules, and gives to the entire organ its smooth, round form. The different lobes have separate secretory ducts, which open upon the nipple. These ducts ramify throughout the substance of the gland tissue, and ultimately carry upon their terminal branches the clusters of secreting vesicles, called acini or alveoli. According to Zocher and Hennig, the true glandular substance has not a rounded shape, but shows a grouping into three principal divisions, one of which extends far up in the direction of the axilla. It is separated from the axillary lymphatic glands only by a small amount of adipose tissue. This would explain the ease, readiness, and frequency with which these glands become implicated in malignant disease of the mamma.

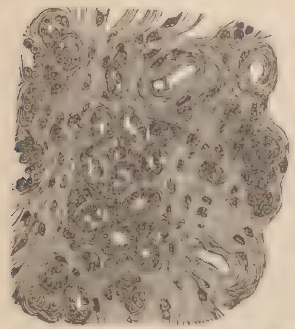

FIG. 189.—Terminal vesicles and stroma from the gland of a nursing woman. Langer.

Since the glands at birth differ very widely from the mammæ of adult women, and still more widely from those of pregnancy, it will be convenient to consider the histology of the organ under different aspects. This will be necessary, however, only with regard to the acini and the epithelia therein implanted, as these alone show such wide morphological divergencies in the different phases of existence.

The *nipple* (teat, *mamilla, papilla mammæ*) is the one structure belonging to the mamma which is least liable to modifications of tissue due to age and sex. It generally assumes the shape of a pigmented conical or cylindrical projection, at the apex of which the galactophorous ducts have their terminal openings. It is composed principally of a rather loosely woven connective tissue, containing abundant corpuscles, and provided

with elastic fibrils. This conjunctive tissue forms a supporting framework for the milk-ducts traversing the nipple. The latter show walls of rather dense fibrous tissue, with a large proportion of elastic elements, and are provided with a lining of one row of short cylindrical cells. As the external orifice is approached, these cells begin to take on the character of the ordinary epidermic corpuscles of the integument. Partsch has found in many animals that the secreting parenchyma accompanied these ducts almost to their mamillary orifices.

The occurrence of unstriped muscle in the nipple, accords with the fact of its erectile properties. But the exact mode of distribution of these elements is still a matter of controversy among histologists. From the researches of Winkler and Kolessnikow, recently confirmed by Partsch, it would appear that they occur not in the ducts themselves, but form an incomplete ring around and external to the same. In or around the smaller galactophorous ducts, muscle-cells cannot be unmistakably recognized, though some authors have described their occurrence there.

As regards the structure of these smaller *galactophorous ducts* (*ductus lactiferi*, milk-ducts) it is quite simple. Their membranous walls consist of a delicate and closely woven reticulum of connective tissue, with a large admixture of fine elastic fibres. Henle, Meckel, and Kolessnikow have described smooth muscle-cells in these canals, but, as already stated, Partsch and others have denied their existence. At any rate, on cross-sections the contracted condition of some of the larger ducts results in a stellate appearance of their lumina, whereas the smaller ducts always appear round or oval.

The larger ducts traced into the gland tissue are found to be provided with saccular dilatations immediately beneath the nipple. These *milk-reservoirs* (*sinus ductuum lactiferorum*, *sacculi lactiferi*, or *ampullæ*) may be 5 to 8 mm. broad, and thus become distinctly perceptible to the naked eye. Below these dilatations the ducts again grow narrower, and by numerous divisions and subdivisions form a system of ramifying tubes, which terminate in the secreting alveoli. The structure of the larger ducts does not materially differ from that of the smaller ones. Their walls are, of course, considerably thicker, and there is found in addition a greater proportion of elastic tis-

sue. All the different kinds of ducts show a lining composed of a single layer of short cylindrical cells, containing ellipsoid nuclei. The character of the lining cells is, however, gradually changed as the acini are approached, near which it merges into the alveolar epithelium by insensible gradations.

Surrounding the nipple is a variously pigmented ring, called the *areola mammæ.* Its surface is slightly corrugated, and this circumstance, taken in connection with its pigmentation, results in the production of the marked contrast it presents to the very white and soft integument covering the other portions of the female mamma. The areola is also provided with abundant unstriped muscle-fibres. Some of the latter surround the nipple in concentric rings, others pursue a radial course. The sudoriferous and sebaceous glands of the areola are conspicuously developed, and lanugo hairs are also found. The familiar changes which go on in the areola simultaneously with the development of pregnancy, are mainly due to increased blood-supply and additional pigmentation. The areola is also provided with small granules of secreting parenchyma. Some of these grains empty the products of their secretory activity by special recurrent ducts into the main excretory canals. But there are others which have special openings upon the free surface of the areola. Usually, little papillary eminences mark the presence of such orifices. These scattered bits of mammary parenchyma are known as the *glandulæ aberrantes* of Montgomery. Kölliker and others regard them as largely developed sebaceous glands.

The *arteries* of the mamma are chiefly derived from the internal mammary artery and the long thoracic. The veins empty into the thoracic branches and cephalic vein. Both arterial and venous vessels proceed subcutaneously from the periphery to the nipple, whence branches are given off in a posterior direction. They are not guided in their course by the distribution of the milk-ducts, but are distributed to the glandular parenchyma in such a way that each lobule has its own separate supply. Finally, under the areola the veins of the nipple form a circular anastomosing chain, known as the *circulus venosus of Haller*. Capillary vessels surround the acini, forming networks with rather close meshes. Of course, the varying states of expansion and contraction in the ultimate alveoli, which conditions correspond to phases of activity and

rest, will materially affect the size and shape of the capillary networks. They are, however, much less distinct and conspicuous during the period of lactation than in the quiescent state of the gland. Rauber found in the glands of pregnant animals that the blood-vessels were not in immediate contact with the walls of the secreting vesicles, being separated from them by interposed lymph-channels. Coyne, Langhans, and Kolessnikow have also described these perialveolar lymph-spaces. Their presence is, indeed, readily demonstrated by injections with nitrate of silver solutions. In actively secreting glands these channels are sometimes packed with leucocytes, which also infiltrate the stroma of the organ.

Lymphatics are plentiful in the mammary gland. We find them subcutaneously, as well as deep in the interior of the organ. Coyne, in 1874, described the perialveolar lymph-spaces, already mentioned, for the human mamma, and Kolessnikow, in 1870, perialveolar lymph-spaces for the mammary gland of the cow. Langhans succeeded in injecting a rich network of periacinal lymph-vessels, likewise lymph-channels around the excretory ducts and the lacteal sinuses. The largest lymph-vessels are retro-glandular. They are without valves. The lymph-vessels of the nipple resemble those of the skin. There seems to be no free communication between the lacunal and interstitial spaces of connective tissue of the glands, and the proper lymph-channels.

The principal lymph-vessels of the mamma, both deep and superficial branches, proceed to the glands of the axilla. But some of the mammary lymphatics also communicate, through intercostal branches, with the thoracic lymphatic glands. These are points worthy of remembrance in studying the mode of dissemination in mammary tumors.

Nerves abound less in the secreting structure of the mamma than in its integumentary apparatus. The majority are of spinal origin, although the sympathetic system is by no means excluded from representation. Branches from the fourth, fifth, and sixth intercostal nerves—the so-called *rami glandulares*—accompany the milk-ducts, and ramify within the organ. Satisfactory evidence concerning the manner of their ultimate termination has, however, not been hitherto obtained. Most of the nerves in the interior of the organ belong to the vascular or vaso-motor variety, and many are seen to accompany the

blood-vessels. Eckhard has given the most elaborate description of the nerve-supply of the human mamma.

Structure of fully expanded gland.—Immediately before, during, and after lactation, the mamma appears as a distinctly lobulated organ, having a pinkish or yellowish hue, and resembling in consistence the human pancreas or salivary gland.

The different lobuli are made up of numerous ultimate acini, having, as a rule, a rounded, pyriform, or slightly polyhedral shape. They are of nearly uniform size, and are closely placed, being separated from one another by only sparing amounts of connective tissue, and the capillary vascular channels therein contained. Elastic fibres and smooth muscle-cells also occur, though not constantly, between the alveoli of the lobules. Lymphoid elements, as well as branched connective-tissue corpuscles, are always encountered there in greater or less abundance. In addition to these elements, large granular corpuscles containing nuclei are found. They are most numerous along the course of the blood-vessels, and appear to be identical with the so-called plasma cells of Waldeyer. Creighton, however, also describes similar cells in the interior of the alveoli, and believes that both are identical, maintaining that they are derived from the acinous epithelium.

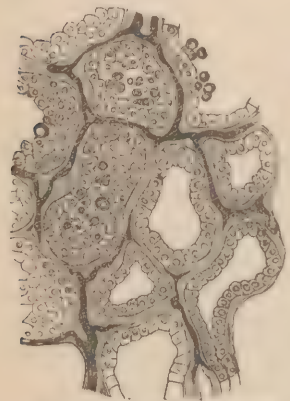

FIG. 190.—Transverse section through the terminal vesicles of the gland in a nursing woman, showing interalveolar capillaries. Langer.

According to this author's description, such cells are "not infrequently seen in the tissue outside a lobule in rows three or four deep; again, they are found in the interfascicular spaces among the lymphoid-cells," that have been already mentioned. These large, granular, and nucleated corpuscles are said to be filled with a bright yellow or golden pigment. Now, Creighton has pointed out that the periodical subsidence of the mammary function is accompanied by the formation of much corpuscular waste material. And the production of these remarkable yellow cells, which finally leave the gland by way of the lymph-vessels, is, according to him, but a final phase of this process.

The mammary epithelium which paves the acini has been variously described as consisting of flat polyhedral (Reinhard);

cubical, cylindrical (Kolessnikow); small polyhedral (Langer); and prismatic (Kehrer) cells. This discrepancy of opinion receives its explanation from the fact that the epithelial cells

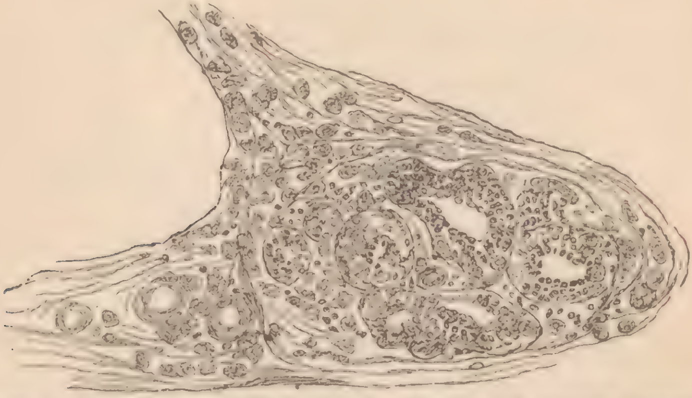

FIG. 191.—Lobule of a mamma near the resting state. Numerous large pigmented cells within the acini and in the interlobular fibrillar tissue. Creighton.

have a different appearance in the various conditions intervening between full activity and complete rest of the gland.

Creighton has given a very satisfactory description of mammary epithelium. He states that in the fully expanded gland "the floor of an acinus in section is covered by a mosaic of polyhedric epithelial cells, usually to the number of fifteen or twenty, while in the larger elongated acini as many as thirty may be counted. The cells are usually pentagonal or hexagonal, and the corners are sometimes rounded. In each cell there is a central round nucleus, which colors brightly with the staining fluid, and a broad fringe of protoplasm, which stains less deeply." The nucleus varies in its relative size, generally having a diameter equal to about one-third that of the entire cell.

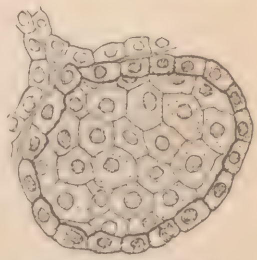

FIG. 192.—Fully expanded acinus, showing mosaic of polyhedral cells. Creighton.

"In a profile view of an acinus, the epithelium appears as a circlet of oblong cells, in which the nucleus at the centre occupies almost the entire thickness of the cell. The mammary epithelial cell may therefore be described as a flattened polyhedric body, with a thickness about one-half of its breadth. The substance of the nucleus is apparently homogeneous, with

a deeper line of staining round the margin; a nucleolus is not always prominently seen."

Structure of involuted mamma.—Having thus briefly indicated the main histological features of a fully evolved gland, we are now prepared to examine the mamma in a condition of advanced involution. By involution, in this sense, is meant the periodical return to inactivity, and not to final retrograde metamorphosis, which culminates in complete senile atrophy. The glandular lobules, then, in the involuted organ are again found to be composed of closely crowded alveoli. But all the lobules appear to have become smaller, and their acinous components are likewise shrunken. The basement-membrane of the latter does not appear to be materially altered, but its cellular contents are considerably changed. In place of the beautiful mosaic characteristic of the active gland, there now appears only an aggregation of nucleated corpuscles to the number of five or ten. Creighton describes them as "nothing else than a somewhat irregular heap of naked nuclei, with no fringe of protoplasm round them, and in size little, if at all, larger than the nucleus alone of the perfect epithelium." This description, however, applies only to hardened specimens, for in fresh preparations the nuclei, as a rule, show a broader or narrower surrounding zone of protoplasm. As regards the diameter of the involuted acini, it is about one-fourth that of the actively secreting alveoli.

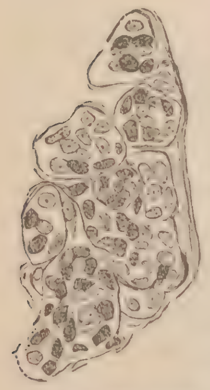

FIG. 193.—Involuted mammary lobule, showing the nuclear contents of the alveoli. Creighton.

Owing to the shrinkage in the glandular parenchyma, the blood-vessels and excretory ducts, as already stated, are more prominent in an involuted than in an active gland.

It is not our purpose here to trace, step by step, the various processes by which a gland passes from the resting state to that condition of complete evolution which is alone compatible with active secretion. For the details of this interesting subject, the reader is referred to the work of Creighton. We may, however, very briefly summarize this author's account of the transformations in question. The one essential circumstance characterizing the whole change is a process of vacuolation, which Creighton assumes to take place in the secreting cells. "The

most definite and unmistakable form of vacuolation is the signet-ring type." This process is, according to him, a true one of endogenous cell formation, resulting in this instance in the formation of milk. Moreover, large, granular, nucleated cells, filled with a bright yellow or golden pigment, "found both within the alveoli and in the interfibrillar spaces without them"

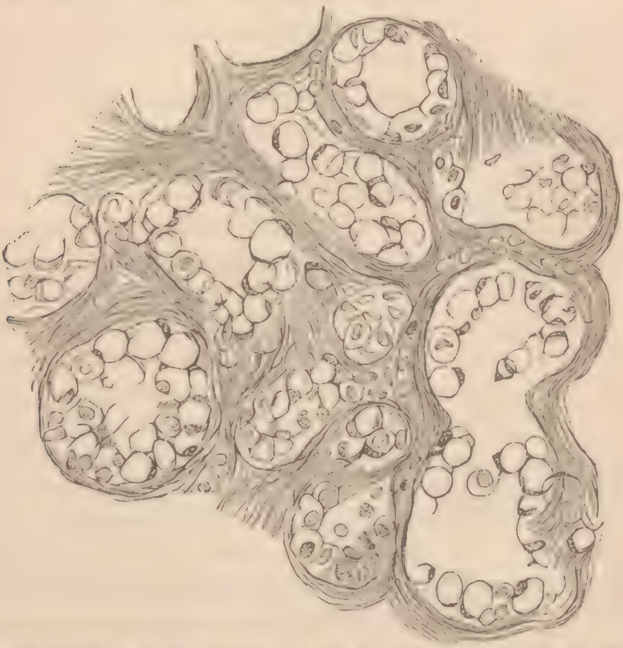

FIG. 194.—Vacuolation of alveolar epithelium. From the udder of a ewe shortly after the end of lactation. The cells *in situ* are vacuolated cells, with the usual thin and, for the most part, uncolored hoop or ring of the vacuole, and the deeply stained peripheral mass. Creighton.

characterize the last stage of involution, "and the pigment that belongs to them is to be found strewn over the lobules that have reached the resting state." Finally, Creighton asserts that "the various forms of cells that characterize the various stages of involution must have resulted from a transformation *de novo* of the renewed epithelium, and not from successive changes upon the same cell." Each epithelial cell, therefore, that is used up in the formation of milk, has been at one time a perfect polyhedral corpuscle or fully equipped cell, and "has rapidly undergone the cycle of changes whereby its whole substance has been converted into milk."

A distinguishing feature of one stage of evolution which

deserves to be mentioned, is "the presence in the cavities of the acini of a peculiar granular material, the coagulated condition of a fluid." Partsch has also described the occurrence of this granular mass within the alveoli, and he states that the secreting epithelia, though of normal size, were furnished with shrunken nuclei, and showed numerous light spots, as if the cells were perforated and sieve-like. It would appear that this writer has observed the stage of vacuolation without, however, interpreting the same in Creighton's sense.

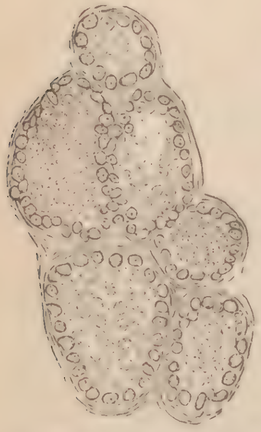

FIG. 195.—Acini from a partly expanded gland, some of them filled with a granular material. From the mamma of a pregnant cat. Creighton.

Creighton also describes in certain glands the connective-tissue stroma as crowded with cellular elements, which he considers equally with the pigmented corpuscles as waste-cells of the secretion. Others (Winkler, Brunn, and particularly Rauber) have assigned a far different significance to these bodies, as will appear farther on. Finally, Creighton explains that the secretion of the mammary gland "may be said to be produced by a transformation of the substance of successive generations of epithelial cells, and in the state of full activity that transformation of the substance is so complete, that it may be called a deliquescence."

Although Creighton's investigations did not extend to the human mammary gland, there is ample ground for the belief that changes of evolution and involution similar to those which he has described in animals, constantly take place in the human female as well. And even if we accept only some of his views on the inter-relations of physiological action and histological appearance, the discrepancy still existing in the descriptions given by different authors will receive a more rational explanation than has hitherto been offered by writers on this subject. Certainly some of his assertions appear rather fanciful in their far-reaching novelty, nevertheless they deserve the attentive consideration which we have, at least, in part bestowed on them.

From the results of our own examinations, we are unable

to concede in all respects the correctness of Creighton's interpretations. The evidences of epithelial destruction for purposes of milk secretion, are not positive and convincing. In the Harderian gland, as well as in the mamma, we have observed the extrusion of fat-droplets from cells replete with them without destruction of the cell itself. Partsch agrees with us in assuming that the cells may burst or otherwise discharge their contents, and yet retain enough protoplasm to maintain their vitality; and also that the vital contractions of the protoplasm may force out the oil-globules without destruction of the epithelium. What Creighton has called vacuolation does not mean death to the cells concerned in this action, for they retain their nuclei and sufficient protoplasm to become re-established as perfect epithelia. That this reformation of old epithelium takes place, is proven by the fact that a new formation by proliferation has never been observed, and by the additional circumstance that the mammary acini never show more than a single layer of lining-corpuscles, and, moreover, always show this layer complete.

In this, as in many other respects, the mamma closely resembles the Harderian gland, more particularly of the rodentia, as described by one of the writers in a monograph. The basement-membrane of the acini in every particular also corresponds in the two kinds of glands, being in both a homogeneous, apparently structureless membrane, with superimposed branched adventitial cells, the so-called *Stützzellen* of German writers. A basket-shaped reticulum, such as has been described by Boll, Langer, Kolessnikow, Moullin, and others, is never found to constitute this *membrana propria*, although artificially, appearances simulating a structure of this kind are readily obtained, and have been interpreted by several histologists as natural occurrences.

In the cutaneous sebaceous glands the secreting vesicles are filled with several superimposed layers of epithelia, and it is this circumstance which leads to an entirely different mode of secretion. For there it would indeed appear that the cells undergoing fatty degeneration become detached from their bases and find their way into the narrow lumen of the acinus. The older or inner generation of cells thus vanishing is replaced by new corpuscles formed by gradual proliferation from the peripheral zone.

Rauber's views on the mamma and the lacteal secretion are somewhat startling, but must occupy our attention here. From a series of very carefully conducted examinations, principally on the glands of guinea-pigs during and after pregnancy, he feels justified in concluding that milk owes its orgin to the entrance of countless leucocytes into the lumen of the gland-vesicles. The emigrated lymphoid elements, he believes, penetrate the alveolar walls, passing through the single layer of epithelial cells which line them. Arrived in the interior of an ultimate acinus, the leucocytes undergo fatty metamorphosis, and thus at length furnish the most essential and characteristic ingredient of milk, viz., the milk-globules. Rauber, therefore, discards the notion that the formed particles of the lacteal secretion originate in the glandular epithelium, and represent the elaborated products of its functional activity. He also denies that previously formed milk globules, or colostrum corpuscles, ever pass through the alveolar walls. Thus the primitive opinion advanced by Empedocles, describing milk as white pus, is in a measure revived, and milk is held to be directly derived from the white corpuscles of the blood.

Preparations of mammary glands taken from animals still suckling their young, according to him, invariably show the intraglandular lymph-vessels replete with leucocytes, the stroma similarly infiltrated, identical corpuscles in greater or less abundance within the vesicles, and transitional forms between lymphoid-corpuscles and milk-globules. These claims, granted to be facts, and considered in conjunction with the circumstance that epithelial proliferation is not seen, would certainly go far to make Rauber's theory seem a somewhat plausible one. Nevertheless, we require corroborative evidence from others, before his views can be accepted as anything more than an ingenious hypothesis.

Rauber has also described the occurrence of a delicate striation within the epithelial cells of the alveoli. These striæ are said to be in all respects similar to those found in the secreting elements of certain portions of the salivary glands and the tubules of the kidneys.

As regards the *corpuscles of Donné*, or *colostrum bodies*, most authors regard them as the products of desquamation of the alveolar epithelium, the latter being in a condition of fatty degeneration (Winkler, De Sinéty, Buchholtz, and others).

Some histologists, like Stricker, hold that oil-globules may be expelled from the interior of fat-filled cells without disintegration of their protoplasmic bodies. It is an undoubtable fact that colostrum corpuscles, when managed with proper precautions, may be seen to yield droplets of fat under the microscope, just as amœbæ reject similar contained particles. Rauber, however, maintains that these bodies represent leucocytes in various stages of fatty metamorphosis, and he calls such corpuscles, when found in the gland vesicles, *galactoblasts.*

In the gland of Harder, one of the writers has found the spacious gland vesicles lined with very large epithelia; and these cells were in many animals entirely fat-filled. They secreted a greasy substance not unlike thick milk. Yet destruction of the cell-body did not occur, at least evidences of such a process could not be obtained. Partsch has therefore anticipated the authors in their conclusion that the secretion of milk is accomplished in much the same way in which the creamy products of the Harderian gland are formed, *i.e.*, without total destruction of epithelial cells. According to our view, then, and it nearly coincides with the opinion of Stricker, Winkler, and especially Partsch, the cells containing the fat-globules may, indeed, burst and discharge their contents, but the nucleus and sufficient protoplasm are retained to enable the epithelium to recuperate, and in the course of time again and again discharge its contents. Along with this mode of milk secretion, a second process occurs. This consists of the gradual extrusion of oil-droplets, the cell body remaining entirely intact, since the mere vital contractions of the protoplasm suffice to drive out one milk-globule after another.

When the activity of the gland is suddenly heightened in the period immediately before childbirth, some few epithelial cells are desquamated. These, appearing in the milk of most women, are identical with the bodies known and described as colostrum corpuscles.

Of other anatomical constituents of normal milk, we only find the *milk-* or *oil-globules.* They are suspended in the fluid emulsion which milk truly represents, in countless numbers. They vary in size from 0.002 to 0.009 mm. A very delicate fringe of protoplasm adheres to their periphery, and it is for this reason that they may appear to become stained when submitted to the action of proper dyes.

DEVELOPMENT OF THE GLAND.

Like the other cutaneous glands of the body, the mamma is first formed by a proliferation inward of certain epidermal cells. In other words, the breast results from a downward extension of epiblastic corpuscles. The first unmistakable indication of the future gland is seen about the third or fourth month of pregnancy. At that time it consists of a solid plug, or pro-

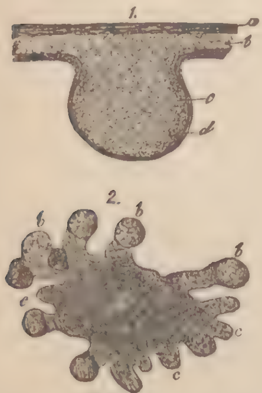

FIG. 196.—1. Rudimentary form of gland in human fœtus: *a*, *b*, epidermis: *c*, aggregation of cells; *d*, connective tissue layer. 2. From a seven-months' fœtus: *a*, central substance; *b*, larger, and *c*, smaller outgrowths. Frey.

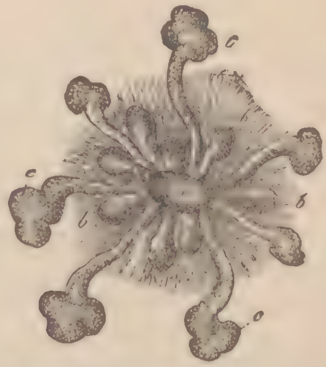

FIG. 197.—Embryonal mamma: *a*, central mass, with *b*. and *c*, variously shaped outgrowths. Frey.

cess, extending downward from the rete-mucosum of the skin. This has been called *Drüsenfeld*, by Huss. From the internal end of this solid process, sprouts, or offshoots, are developed, and they represent the future separate glands constituting the mature organ. These buds have a pyriform, or club-like shape, and are surrounded by ordinary embryonal connective tissue. The further growth of the gland takes place by a process of continuous extension and subdivision, but indications of the latter are not always found at birth. Ducts are already visible in the new-born infant, but the aggregations of cells representing the future acini, remain without lumina for a much longer period.

Th. Kölliker describes as a constant occurrence, especially marked in the breasts of female infants, the dilatation of a greater or smaller number of milk-ducts. Such ectatic-canals

have their lumina filled with desquamated epithelial cells, and a whitish, granular material. Formerly, these occurrences were considered to be exceptional, and were regarded as having a pathological significance. During the first year of extra-uterine life, this characteristic process of progressive dilatation may assume such large dimensions, that the mamma may come to resemble cavernous tissue, the ectatic spaces of which are paved with flattened epithelium. Within certain limits, Kölliker regards this as a perfectly normal physiological event. But he adds that an exaggerated process of this kind may result in early mastitis. Such an occurrence, he thinks, may explain the rudimentary development of the breasts observed in some women of otherwise normal growth.

The post-embryonal growth of the mamma has been carefully studied by Langer, and his results and conclusions having been confirmed by the investigations of Kölliker, Huss, and others, must still be received as representing the true condition of things, in spite of the novel and heterodox views advanced by Creighton.

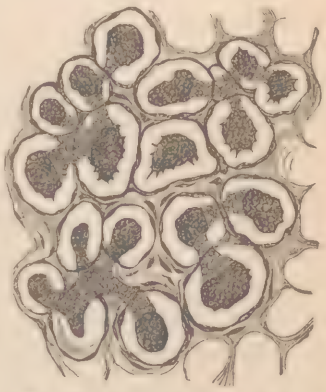

FIG. 198.—Transverse section of glandular vesicles in a virgin. Langer.

Up to the time of puberty, the growth of the breast is very gradual and quite insignificant, even in females. Then, however, the ducts begin to rapidly ramify in all directions, and, by offshoots from various points, true acini are at length developed. But they remain of small size until the stimulus of pregnancy causes a further evolution. In the male, the existing ducts, as a rule, atrophy with advancing age. The evolution changes which the mamma undergoes during pregnancy, have already been set forth, and there remain to be considered only those final phases of metamorphosis which take place in the climacteric period of life.

These are readily understood, consisting essentially of a complete atrophy of all the secreting acini. Simultaneously with these atrophic changes the epithelia of the galactophorous ducts become flattened, and finally shrink, so as to form only squamous plates, which line the ramifying processes of connec-

tive tissue representing the former lactiferous canals. The terminal portions of these larger duct-remnants are sometimes connected with minute channels, the latter being the remnants of collapsed smaller ducts. In some measure we find a compensatory production of fat, which partly replaces the faded acini. The breasts of old women, therefore, consist of fibrous tissue, with a large proportion of elastic elements, fat-cells, and the remnants of the ducts. It may be remarked that the latter frequently show cystic dilatations, the cavities being filled with a dirty, slimy fluid. The blood and lymph-vessels, but especially the latter, participate in the general atrophy of the tissues.

This succinct account concerning the histogenesis of the mammary gland, does not, as already intimated, represent the unchallenged opinion on its first development. For Creighton, in the remarkable work already cited, radically opposes the view that the mamma takes its origin from the epiblast. He believes, on the contrary, that it starts from the mesoblast, or connective-tissue layer of the embryo, and not the upper epithelial layer or epiblast. According to him, moreover, and his conclusions are based on developmental studies, chiefly of the guinea-pig's gland, the process may be justly described as a centripetal one, whereas the current view represents this gland-develpoment as essentially centrifugal. We have already expressed our adherence to the current view, attributing this growth to extension from a central point. Nevertheless, it seems proper to briefly give the conclusions of Creighton, especially since they appear to be singularly corroborative of the account given by Goodsir of this process, as early as 1842, an account which has apparently remained almost unnoticed by workers in this branch of scientific medicine.

Creighton then concludes his inquiry as follows:

"1. The mammary acini of the guinea-pig develop at many separate points in a matrix-tissue. The embryo cells from which they develop are of the same kind that give origin to the surrounding fat-tissue. The process of development of the mammary acini is, step-for-step, the same as that of the fat-lobules."

"2. The ducts of the mamma develop from the same matrix-tissue, by direct aggregation of the embryonic-cells, along predetermined lines. The ducts develop, in the individual guinea-pig, before the acini, whereas, in the phylogenetic suc-

cession, the ducts are a later acquisition. This reversal of the order of acquisition of parts is in accordance with the principle stated by Herbert Spencer, that 'under certain circumstances the direct mode of development tends to be substituted for the indirect.'"

Hints regarding the histological study of the mamma.— The evolution of the mammary structure progresses *pari passu* with the development of its functional activity. It is the stimulus of pregnancy which determines both. Nevertheless, even during the period of its fullest physiological bloom, *i.e.*, during lactation, variations in the degree of functional activity normally take place. Moreover, the same gland may contain lobules which are comparatively at rest, and others which are at the full height of activity. This should always be borne in mind in interpreting the results of histological inspection of this organ, lest erroneous impressions be conveyed.

The alveolar epithelial cells will, therefore, not be found alike in the different acini, nor yet even in the same vesicle. We may find cuboidal cells, and cylindrical ones, and flattened corpuscles, and in addition, various transitional forms between these types.

The nucleus will appear round, or oval, and about 6–7 μ in diameter. Sometimes two nuclei may be found in one cell. The radiating striation observed by Rauber in many cells, has already received mention. It is a noteworthy fact that the cells themselves contain only a very small proportion of fatty granules, whereas the intra-alveolar lumen is often replete with the same.

In order, then, to study the histology of the gland at the high-water-mark of its functional activity, animals should be chosen which have either just given birth to their young, or are about to do so. For the normal conditions of the human mamma are rapidly transformed by post-mortem change, if not previously altered in consequence of the disease which caused the death of the individual. The organ may be examined fresh, or else hardened and then cut in sections to be stained and mounted in the ordinary manner.

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